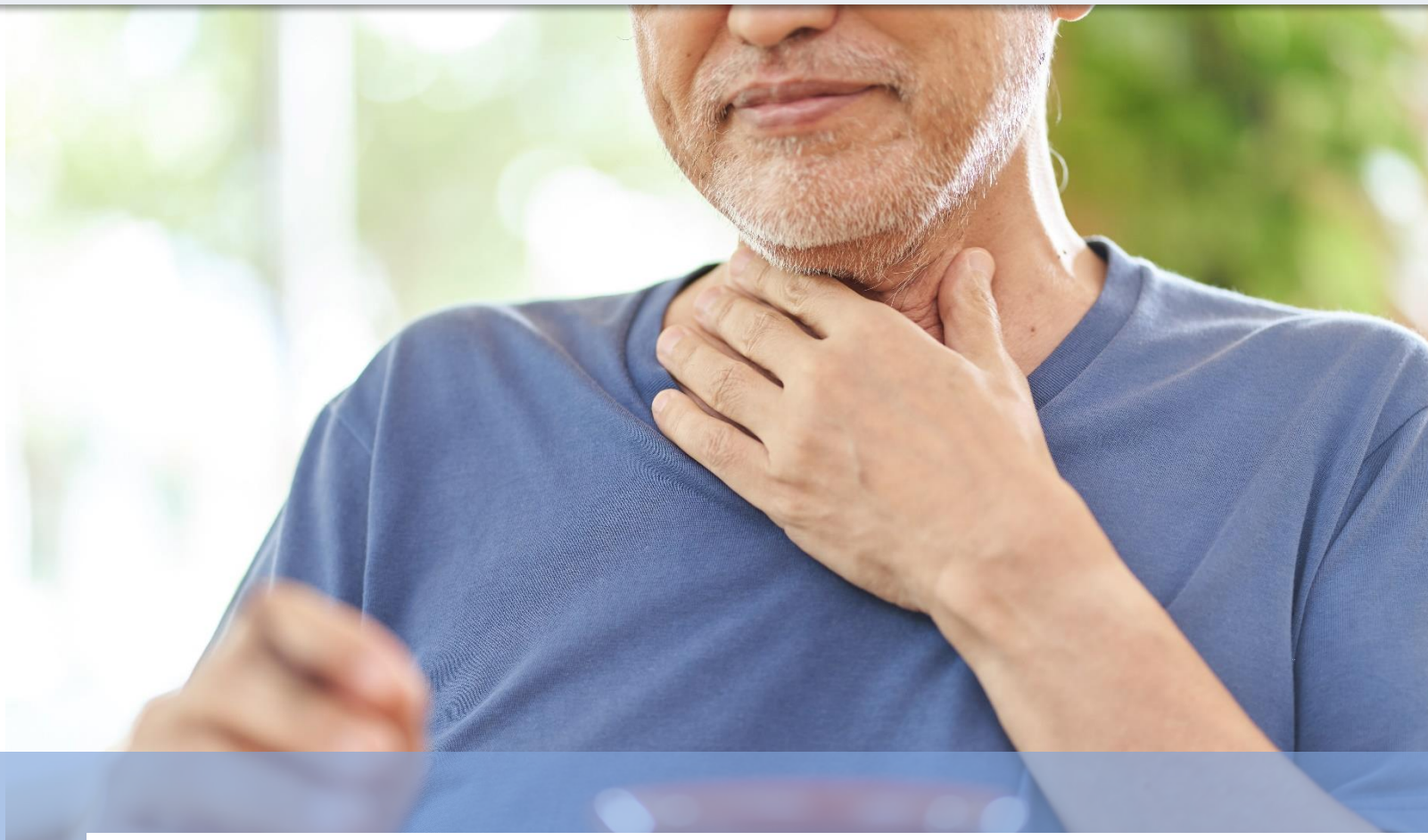
ERABI EVIDENCE-BASED REVIEW of moderate to severe ACQUIRED BRAIN INJURY



DYSPHAGIA, ASPIRATION, AND NUTRITIONAL INTERVENTIONS

POST ACQUIRED BRAIN INJURY

Penny Welch-West M.Cl.Sc. SLP, Sarvenaz Mehrabi MD MSc, Cecilia Flores-Sandoval PhD, Peiwen Cao MSc, Amber Harnett MSc RN, Amanda Dufault MScFN, RD, Robert Teasell MD FRCPC

Disclaimer

This review has been prepared based on the scientific and professional information available up to May 2022. The ERABI information is provided for informational and educational purposes only. If you have or suspect you have a health problem, you should consult your health care provider. The ERABI contributors shall not be liable for any damages, claims, liabilities, costs, or obligations arising from the use or misuse of this material.

Copyright

Funding

This work is funded by the Ontario Ministry of Health. All work produced by ERABI is editorially independent from its funding source.

Conflict of Interest

In the context of ERABI development, the term “conflict of interest” (Bruder et al.) refers to situations in which an author or ERABI staff member’s financial, professional, intellectual, personal, organizational or other relationships may compromise their ability to independently conduct this evidence-based review. No limiting conflicts were identified.

Contact Information

Evidence-Based Review of Moderate to Severe Acquired Brain Injury

550 Wellington Rd South, London, Ontario, Canada N6C 0A7

Website: www.ERABI.ca

Greetings from Dr. Robert Teasell,

Professor and Chair-Chief of Physical Medicine and Rehabilitation

The Collaboration of Rehabilitation Research Evidence (CORRE) team is delighted to present the Evidence-Based Review of moderate to severe Acquired Brain Injury (ERABI) *Dysphagia, Aspiration and Nutritional Interventions Post Acquired Brain Injury.* Through collaboration of researchers, clinicians, administrators, and funding agencies, ERABI provides an up-to-date review of the current evidence in brain injury rehabilitation. ERABI synthesizes the research literature into a utilizable format, laying the foundation for effective knowledge transfer to improve healthcare programs and services.

We offer our heartfelt thanks to the many stakeholders who are able to make our vision a reality. Firstly, we would like to thank the Ontario Neurotrauma Foundation, which recognizes ERABI's capacity to lead in the field of brain injury evidence-based reviews and is committed to funding it. We would also like to thank the co-chairs of ERABI, Dr. Mark Bayley (University of Toronto) and Dr. Shawn Marshall (University of Ottawa) for their invaluable expertise and stewardship of this review. Special thanks to the authors for generously providing their time, knowledge and perspectives to deliver a rigorous and robust review that will guide research, education and practice for a variety of healthcare professionals. We couldn't have done it without you! Together, we are building a culture of evidence-based practice that benefits everyone.

We invite you to share this evidence-based review with your colleagues, patient advisors that are partnering within organizations, and with the government agencies with which you work. We have much to learn from one another. Together, we must ensure that patients with brain injuries receive the best possible care every time they require rehabilitative care – making them the real winners of this great effort!

Robert Teasell, MD FRCPC

TABLE OF CONTENTS

Preface

About the Authors

ERABI is internationally recognized and led by a team of clinicians and researchers with the goal of improving patient outcomes through research evidence. Each ERABI module is developed through the collaboration of many healthcare professionals and researchers.

Penny Welch-West is a medical Speech-Language Pathologist who enjoys a varied clinical practice ranging from Rehabilitation through Complex/Continuing and Palliative Care. Her work includes teaching, assessment and treatment in the areas of dysphagia (swallowing), voice, articulation, language, cognitive-communication and Augmentative and Alternative Communication (AAC). Penny holds an Adjunct Clinical Professor position with McMaster University and a Lecturer position with Western where she teaches in AAC and Traumatic Brain Injury.

Sarvenaz Mehrabi, MD, MSc is a clinical research assistant at the CORRE Lab. She completed a Master's degree in Health Promotion at Western University. She is passionate about improving evidence-based practice through clinical research and promotion public health through health service and strategy research.

Cecilia Flores-Sandoval, PhD, is the research coordinator of the Evidence-Based Review of Acquired Brain Injury (ERABI). She completed a master's degree and a PhD in Health and Rehabilitation Sciences, field of Health and Aging. Her research interests include aging and rehabilitation, patient engagement and transitional care for older adults.

Peiwen Cao, MSc, is the research coordinator of the Spinal Cord Injury Research Evidence (SCIRE). She has a background in health sciences and psychology. Her research interests focus on the psychosocial aspect of physical disabilities.

Amber Harnett, MSc, RN, CNF scholar, completed her MSc in pathology at Western University and the accelerated BScN program at Western University. Passionate about supporting and advocating for those with brain injuries, she also works as a research coordinator to improve the rehabilitation system through research synthesis, guideline development, knowledge translation, education and outreach, in the CORRE lab at Parkwood Institute.

Amanda Dufault, MScFN, RD, is a Registered Dietitian currently working with a diverse set of patients within Complex Care and Palliative Care inpatient programs at Parkwood Hospital. Her work includes nutrition screening, assessment and treatment in the areas of stroke, brain injuries, dysphagia, enteral feeding, malnutrition, diabetes, chronic kidney disease, hemodialysis/peritoneal dialysis, etc. She has completed her Masters of Science in Food and Nutrition at Western University where her area of research focused on sarcopenia in community dwelling and institutionalized elderly.

Dr. Robert Teasell is a Professor of Physical Medicine and Rehabilitation, Schulich School of Medicine and Dentistry, Western University and a Clinical Researcher at Lawson Research Institute in London, Ontario. He is a clinician at Parkwood Institute, St. Joseph's Health Care London.

Purpose

The Evidence-Based Review of Acquired Brain Injury (ERABI) is a systematic review of the rehabilitation literature of moderate to severe acquired brain injuries (Merimee & Rabin). It is an annually updated, freely accessible online resource that provides level of evidence statements regarding the strength of various rehabilitation interventions based on research studies. The ERABI is a collaboration of researchers in London, Toronto and Ottawa. Our mission is to improve outcomes and efficiencies of the rehabilitation system through research synthesis, as well as from providing the foundational research evidence for guideline development, knowledge translation, and education initiatives to maximize the real-world applications of rehabilitation research evidence.

Key Concepts

Acquired Brain Injury

For the purposes of this evidence-based review, we used the definition of ABI employed by the Toronto Acquired Brain Injury Network (2005). ABI is defined as damage to the brain that occurs after birth and is not related to congenital disorders, developmental disabilities, or processes that progressively damage the brain. ABI is an umbrella term that encompasses traumatic and non-traumatic etiologies.

TABLE 1 | Defining Acquired Brain Injury

Included in ABI definition	Excluded from ABI definition
Traumatic Causes • Motor vehicle accidents • Falls • Assaults • Gunshot wounds • Sport Injuries **Non-traumatic Causes** • Tumours (benign/meningioma only) • Anoxia • Subarachnoid hemorrhage (non-focal) • Meningitis • Encephalitis/encephalopathy (viral, bacterial, drug, hepatic) • Subdural Hematoma	**Vascular and Pathological Incidents** • Intracerebral hemorrhage (focal) • Cerebrovascular accident (i.e., stroke) • Vascular accidents • Malignant/metastatic tumours **Congenital and Developmental Problems** • Cerebral Palsy • Autism • Developmental delay • Down's syndrome • Spina bifida with hydrocephalus **Progressive Processes** • Alzheimer's disease • Pick's disease • Dementia • Amyotrophic Lateral Sclerosis • Multiple Sclerosis • Parkinson's disease • Huntington's disease

Given that 'ABI' can have multiple definitions, studies with an 'ABI' population can be equally heterogeneous in terms of the sample composition. Such studies may include any combination of persons with TBI, diffuse cerebrovascular events (i.e., subarachnoid hemorrhage) or diffuse infectious disorders (i.e., encephalitis or meningitis). The vast majority of individuals with ABI have a traumatic etiology; therefore, much of the brain injury literature is specific to TBI. The terms ABI and TBI have been used intentionally throughout ERABI to provide more information about populations where relevant.

Moderate to Severe Brain Injury

ABI severity is usually classified according to the level of altered consciousness experienced by the patient following injury (Table 2). The use of level of consciousness as a measurement arose because the primary outcome to understand the severity of an injury is the Glasgow Coma Scale. Consciousness levels following ABI can range from transient disorientation to deep coma. Patients are classified as having a mild, moderate or severe ABI according to their level of consciousness at the time of initial assessment. Various measures of altered consciousness are used in practice to determine injury severity. Common measures include the Glasgow Coma Scale (GCS), the duration of loss of consciousness (LOC), and the duration of post-traumatic amnesia (PTA). Another factor used to distinguish moderate and severe brain injury is evidence of intracranial injury on conventional brain imaging techniques which distinguish severity of injury from a mild or concussion related brain injury.

TABLE 2 | Defining Severity of Traumatic Brain Injury, adapted from Veterans Affairs Taskforce (2008) and Campbell (2000)

Criteria	Mild	Moderate	Severe	Very Severe
Initial GCS	13-15	9-12	3-8	Not defined
Duration LOC	< 15minutes*	<6 hours	6-48 hours	>48 hours
Duration PTA	< 1hour*	1-24 hours	1-7 days	>7 days
	*This is the upper limit for mild traumatic brain injury; the lower limit is any alteration in mental status (dazed, confused, etc.).			

Methods

An extensive literature search using multiple databases (CINAHL, PubMed/MEDLINE, Scopus, EMBASE, and PsycINFO) was conducted for articles published in the English language between 1980–May 2022 that evaluate the effectiveness of any intervention/treatment related to ABI. The references from key review articles, meta-analyses, and systematic reviews were reviewed to ensure no articles had been overlooked. For certain modules that lacked research evidence the gray literature, as well as additional databases, were searched in order to ensure the topic was covered as comprehensively as possible.

Specific subject headings related to ABI were used as the search terms for each database. The search was broadened by using each specific database's subject headings, this allowed for all other terms in the database's subject heading hierarchy related to ABI to also be included. The consistent search terms used were "head injur*", "brain injur*", and "traumatic brain injur*". Additional keywords were used specific to each module. A medical staff librarian was consulted to ensure the searches were as comprehensive as possible.

Every effort was made to identify all relevant articles that evaluated rehabilitation interventions/ treatments, with no restrictions as to the stage of recovery or the outcome assessed. For each module, the individual database searches were pooled, and all duplicate references were removed. Each article title/abstract was then reviewed; titles that appeared to involve ABI and a treatment/intervention were selected. The remaining articles were reviewed in full.

Studies meeting the following criteria were included: (1) published in the English language, (2) at least 50% of the study population included participants with ABI (as defined in Table 1) or the study independently reported on a subset of participants with ABI, (Dickerson et al.) at least three participants, (4) ≥50% participants had a moderate to severe brain injury (as defined in Table 2), and (5) involved the evaluation of a treatment/intervention with a measurable outcome. Both prospective and retrospective studies were considered. Articles that did not meet our definition of ABI were excluded.

Interpretation of the Evidence

The levels of evidence (Table 3) used to summarize the findings are based on the levels of evidence developed by Sackett et al. (2000). The levels proposed by Sackett et al. (2000) have been modified; specifically, the original ten categories have been reduced to five levels. Level 1 evidence pertains to high quality randomized controlled trials (RCTs) (PEDro ≥6) and has been divided into two subcategories, level 1a and level 1b, based on whether there was one, or more than one, RCT supporting the evidence statement.

The evidence statements made in evidence-based reviews are based on the treatment of groups rather than individuals. There are times when the evidence will not apply to a specific case; however, the majority of patients should be managed according to the evidence. Ultimately, the healthcare professional providing care should determine whether an intervention is appropriate and the intensity with which it should be provided, based on their individual patient's needs. Furthermore, readers are asked to interpret the findings of studies with caution as evidence can be misinterpreted. The most common scenario occurs when results of a trial are generalized to a wider group than the evidence allows. Evidence is a tool, and as such, the interpretation and implementation of it must always be done with the known limitations in mind.

TABLE 3 | Levels of Evidence

Level	Research Design	Description
1A	Randomized Controlled Trial (RCT)	More than one RCT with PEDro score ≥6. Includes within subject comparisons, with randomized conditions and crossover designs
1B	RCT	One RCT with PEDro ≥6
2	RCT	One RCT with PEDro <6
	Prospective Controlled Trial (PCT)	Prospective controlled trial (not randomized)
	Cohort	Prospective longitudinal study using at least two similar groups with one exposed to a particular condition
3	Case Control	A retrospective study comparing conditions including historical controls
4	Pre-Post Trial	A prospective trial with a baseline measure, intervention, and a post-test using a single group of subjects
	Post-test	A prospective intervention study using a post intervention measure only (no pre-test or baseline measurement) with one or more groups
	Case Series	A retrospective study usually collecting variables from a chart review
5	Observational study	Using cross sectional analysis to interpret relations
	Clinical Consensus	Expert opinion without explicit critical appraisal, or based on physiology, biomechanics or “first principles”
	Case Reports	Pre-post or case series involving one subject

Strength of the Evidence

The methodological quality of each randomized controlled trial (RCT) was assessed using the Physiotherapy Evidence Database rating scale developed by the Centre for Evidence-Based Physiotherapy in Australia (Moseley et al., 2002). The PEDro is an 11-item scale; a point is awarded for ten satisfied criterion yielding a score out of ten. The first criterion relates to external validity, with the remaining ten items relating to the internal validity of the clinical trial. The first criterion, eligibility criteria, is not included in the final score. A higher score is representative of a study with higher methodological quality.

DYSPHAGIA, ASPIRATION, AND NUTRITIONAL INTERVENTIONS

POST ACQUIRED BRAIN INJURY

Summary of the Evidence

Intervention	Key Points Level of Evidence
Dysphagia	
Interventions for Dysphagia Management	Intensified facial-oral tract therapy in swallowing may improve swallowing specific parameters in patients with ABI. - *There is level 1b evidence (Jakobsen et al., 2019) that intensified facial-oral tract therapy in swallowing is feasible and may improve swallowing specific parameters in individuals with ABI.* Evidence-based bundled cared may be effective for improving swallowing function post TBI. - *There is level 2 evidence (Yan et al. 2021) that evidence-based bundle may improve swallowing function in individuals with severe TBI.* An intensive rehabilitation program for communicative and swallowing disorders may be effective in treating dysphagia and dysarthria in patients with anoxic brain injury. - *There is level 4 evidence (Nordio et al., 2019) that an intensive rehabilitation program for communicative and swallowing disorders may be effective in treating in individuals with anoxic brain injury.*
Oral Health	
Oral Health Interventions	Oral hygiene education may result in a decrease in dental plaque. - *There is level 2 evidence (Zasler et al., 1993) that providing oral hygiene education to individuals post TBI results in a significant reduction of dental plaque, measured by the Plaque Index Score.* Enhanced oral care may reduce the rate of non-ventilator in hospital pneumonia in brain injured patients. - *There is level 3 evidence (Robertson & Carter, 2013) that enhanced oral care may reduce rates of non-ventilator hospital-acquired pneumonia compared to standard oral care in mixed brain injury populations.* Decontamination of oropharyngeal tract using povidone-iodine may not prevent ventilator-associated pneumonia in in ICU admitted brain injured patients. - *There is level 1b evidence (Seguin et al., 2014) that povidone-iodine is not more effective for reducing the incidence of ventilator-associated pneumonia compared to placebo in individuals post stroke or ABI.*
Nutritional Interventions	

Intervention	Key Points Level of Evidence
Enteral Nutrition	The evidence regarding which method of feeding (EN or PN) is optimal to deliver nitrogen, meet required energy expenditures, nutritional goals and prevent complications. - *There is level 1b evidence (Carteron et al., 2021) that both hypocaloric polymeric EN regimen and Hypercaloric semi-elemental EN regimen had the same effect of nutritional outcomes including albumin and pre-albumin levels, except for the daily protein intake level which was higher in hypercaloric semi-elemental EN regimen post TBI.* - *There is level 1b evidence (Zhang et al., 2020) that EN combined with PN for individuals with TBI showed greater improvement in the levels of hemoglobin, albumin, pre-albumin, total protein, and the outcomes, and lower rates of adverse effects and complications, when compared to just EN administration.* - *There is level 2 evidence (Justo Meirelles & de-Aguilar-Nascimento, 2011) that TPN delivered nitrogen more efficiently than EN therapy in individuals post TBI. However, both groups showed a significant improvement in nitrogen balance as a result of nutritional therapy.* - *There is level 2 evidence (Nataloni et al., 1999) that enteral feeding may be effective for improving nitrogen balance, while also increasing serum pre-albumin and RBP levels compared to parenteral nutrition and enteral plus parenteral nutrition in individuals post head injury.* - *There is level 2 evidence (Borzotta et al., 1994) that individuals post closed head injury treated with TPN or EN had no differences in nitrogen balance, energy expenditures, meeting nutritional goals and frequency of infections. However, enteral feeding post ABI may lead to decreased rates of hyperglycemia and diarrhea compared to parenteral nutrition.* - *There is level 2 evidence (Young et al., 1987) that intracranial pressure and serum osmolality are not affected by TPN or EN interventions in individuals post severe head injury.* - *There is level 2 evidence (Hadley et al., 1986) that individuals post TBI treated with NG or PTN had no significant changes in nitrogen balance, although, NG may be more effective in reducing nitrogen intake and nitrogen loss, when compared to PTN.* - *There is level 2 evidence (Rapp et al., 1983) that enteral feeding may reduce mean intake of nitrogen compared to parenteral nutrition in individuals post head injury.* - *There is level 4 evidence (Chapple et al., 2016) that enteral feeding may be effective for meeting energy and protein requirements, while also contributing to a smaller protein deficit, compared to oral feeding in individuals post TBI.* - *There is level 2 evidence (Fan et al., 2016) that enteral feeding may increase serum protein, the rate of aspirated pneumonia and diarrhea when compared to parenteral nutrition or combined enteral-parenteral nutrition post ABI.* Enteral nutrition with high protein formulas may improve FIM motor and cognitive scores and result in less weight loss. - *There is level 2 evidence (Horn et al., 2015) that standard enteral nutrition or high protein formulas (greater than 20% of calories from protein) resulted in better FIM motor and FIM cognitive scores at discharge and less weight loss than similar patients not receiving enteral nutrition post TBI.*

Intervention	Key Points Level of Evidence
	For those with ABI being provided with enteral nutrition, energy expenditure levels may be beyond those predicted by equations. - *There is level 4 evidence (Clifton et al., 1984) that individuals post head injury may expend more energy when on enteral nutrition than predicted by equations, and that this effect may be greater for non-sedated individuals.* Enteral feeding may help to improve required interstitial brain glucose for people with severe brain injuries. - *There is level 4 evidence (Kofler et al., 2018) that EN improved interstitial brain glucose levels in individuals with poor-grade sub-arachnoid hemorrhage, and this method of nutrition administration can be implied in the glucose management in these patients.*
Enteral Nutrition Timing	Early enteral nutrition may be more beneficial than standard or late enteral nutrition for several patient outcomes post ABI, including survival and disability outcomes. - *There is level 1b evidence (Chourdakis et al., 2012) that early enteral nutrition may improve the hormonal profile of individuals post TBI compared to delayed enteral feeding.* - *There is level 2 evidence (Minard et al., 2000) that early versus late enteral feeding has a similar effect on mortality, number of infections, ventilator days, or incidence of pneumonia in individuals post TBI.* - *There is level 2 evidence (Taylor & Fettes, 1998) that early enteral nutrition may improve energy and nitrogen intake compared to standard enteral nutrition in individuals post head injury.* - *There is level 2 evidence (Ohbe et al., 2020) that early enteral nutrition may result in lower incidence of nosocomial pneumonia than late enteral nutrition.* - *There is level 2 evidence (Azim et al., 2016) that early and late enteral feeding did not have different impacts on mortality, general complications, ventilator days, hospital length of stay, and GCS at discharge. However, it was shown that early enteral feeding may result in longer length of stay in ICU, and higher rates of pneumonia.* - *There is level 2 evidence (Dhandapani et al., 2012) that late total enteral feeding can result in reduced arm circumference, worse malnutrition, and more disability compared to early total enteral feeding in individuals post TBI.*
Enteral Nutrition Administration Strategies	Selective surgical feeding tube placement strategies can reduce the number of unnecessary surgical feeding tubes and subsequent complications post-ABI. - *There is level 2 evidence (Marcotte et al., 2018) that a specific surgical feeding tube placement strategy can reduce the number of unnecessary surgical feeding tube placements and subsequent complications in individuals post ABI.*

Intervention	Key Points Level of Evidence
Enhanced Feeding Solutions	Immune-enhanced EN regimens may result in lower rates of inflammation and infection, and better recovery. However, there is conflicting evidence as to whether immune enhanced EN solutions reduce ventilator dependency, and hospital length of stay in patients post-ABI. - *There is level 1b evidence (Wan et al., 2020) that probiotics combined with early enteral nutrition may reduce serum levels of ET-1, CRP, and IL-6, IL-10, and TNF-α and facilitate recovery in patients with severe TBI.* - *There is level 2 evidence (Wandrag et al., 2019) that although administering Leucine-enriched essential amino acid to patients with TBI may be feasible, there are significant barriers to measurement of the intervention outcomes.* - *There is level 1b evidence (Jia et al., 2018) that sequential enhanced enteral feeding may increase protein levels and GCS scores 14 days post-treatment in patients post ABI.* - *There is level 1b evidence (Falcao de Arruda & Aguilar-Nascimento, 2004) that glutamine- and probiotics-enhanced diet may reduce infection rates, length of stay, and ventilator days compared to standard diet in patients post TBI.* - *There is level 2 evidence (Taylor et al., 1999) that enhanced enteral feeding may result in higher energy and nitrogen requirements compared to standard enteral feeding, but fewer infections and earlier discharge in patients post head injury.* - *There is level 2 evidence (Painter et al., 2015) that immune enhancing nutrition may result in longer length of stay and ventilator days compared to standard formula, but lower risk of bacteremia in patients post TBI.* Protein-enhanced EN regimens may be helpful for those who have elevated protein needs but lower caloric needs. - *There is level 4 evidence (Buckley et al., 2021) that protein-enhanced EN regimen could improve the protein intake without any increase in the calory intakes in patients on propofol therapy.*
Metoclopramide	The use of metoclopramide to aid in gastric emptying may not be effective in individuals with TBI. - *There is level 1b evidence (Nursal et al., 2007) that metoclopramide may not be effective compared to placebo for gastric emptying in patients post TBI.*
Total Parenteral Nutrition	
Total Parenteral Nutrition	Parenteral nutrition with a continuous infusion of insulin may lower blood glucose levels in ABI populations. - *There is level 1b evidence (Mousavi et al., 2014) that insulin infusions significantly decrease blood glucose levels in patients post TBI.*

Intervention	Key Points Level of Evidence
	The evidence regarding which method of feeding (EN or PN) is optimal to deliver nitrogen, meet required energy expenditures, nutritional goals and prevent complications (e.g., diarrhea and pneumonia) is conflicting. Further research is needed to clarify the effect of both feeding routes on nitrogen balance post ABI. - *There is level 2 evidence (Justo Meirelles & de-Aguilar-Nascimento, 2011) that TPN delivered nitrogen more efficiently than EN therapy in patients post TBI. However, both groups showed a significant improvement in nitrogen balance as a result of nutritional therapy.* - *There is level 2 evidence (Nataloni et al., 1999) that EN may be effective for improving nitrogen balance compared to PN and EN+PN in patients post head injury.* - *There is level 2 evidence (Borzotta et al., 1994) that patients post closed head injury treated with TPN or EN had no differences in nitrogen balance, energy expenditures, meeting nutritional goals and frequency of infections. However, EN may lead to decreased rates of hyperglycemia and diarrhea compared to PN.* - *There is level 2 evidence (Young et al., 1987) that intracranial pressure and serum osmolality are not affected by TPN or EN interventions in patients post severe head injury.* - *There is level 2 evidence (Hadley et al., 1986) that patients post TBI receiving NG or TPN had no significant changes in nitrogen balance, although, NG may be more effective in reducing nitrogen intake and nitrogen loss, when compared to TPN.* - *There is level 2 evidence (Hausmann et al., 1985) that PN reduces the amount of regurgitated gastric fluid compared to combined EN+PN, however, nitrogen balance could not be reached for either PN or combined EN and PN in patients post ABI.* - *There is level 2 evidence (Rapp et al., 1983) that EN may reduce mean intake of nitrogen compared to PN in patients post head injury.* - *There is level 2 evidence (Fan et al., 2016) that EN may increase serum protein, the rate of aspirated pneumonia and diarrhea when compared to PN or combined EN+PN in patients post ABI.* Using carbohydrate as the only source of energy in TPN regimen may cause fatty acids deficiency. - *There is level 1b evidence (Adolf et al., 1995) that using carbohydrate as the only source of energy in TPN regimens results in fatty acids deficiency.*
Total Parenteral Nutrition Timing	Early parenteral nutrition support may improve immunologic function in individuals with ABI. - *There is level 2 evidence (Sacks et al., 1995) that early parenteral nutrition support may improve immunologic function compared to delayed parenteral nutrition in patients post ABI.*
Combined Nutrition	

Intervention	Key Points Level of Evidence
Combined Nutritional Interventions	The evidence is conflicting regarding which method of feeding (EN or PN or combined EN + PN) is optimal to deliver nitrogen, meet required energy expenditures, nutritional goals, facilitate recovery, and prevent complications (e.g., diarrhea and pneumonia). Further research is needed to clarify the effect of combined feeding routes on nitrogen balance post ABI. - *There is level 1b evidence (Zhang et al., 2020) that EN combined with PN for individuals with TBI showed greater improvement in the levels of hemoglobin, total protein, and the outcomes, and lower rates of adverse effects and complications, when compared to just EN administration.* - *There is level 2 evidence (Nataloni et al., 1999) that patients post head injury treated with TPN or EN had no differences in nitrogen balance, energy expenditures, meeting nutritional goals and frequency of infections. However, enteral feeding may lead to decreased rates of hyperglycemia and diarrhea compared to parenteral nutrition.* - *There is level 2 evidence (Hausmann et al., 1985) that parenteral nutrition reduces the amount of regurgitated gastric fluid compared to combined enteral and parenteral nutrition; however, nitrogen balance could not be reached for either PN or combined EN and PN in patients post ABI.* - *There is level 2 evidence (Li et al., 2022) that combined EN and PN may lead to lower Incidence of lung infection and greater improvement in GCS score in patients with TBI with GCS≤8 at admission compared to PN alone.* - *There is level 2 evidence (Fan et al., 2016) that enteral feeding post ABI may increase serum protein, the rate of aspirated pneumonia and diarrhea when compared to parenteral nutrition or combined enteral-parenteral nutrition in patients post ABI.* Combined enteral-parenteral nutrition post ABI may promote nutritional independence by 6 months post injury. - *There is level 4 evidence (Krakau et al., 2007) that combined enteral-parenteral nutrition may facilitate nutritional independence within the first six months post TBI.* The utilization of multiple nutritional intervention strategies and an interdisciplinary approach to treatment may result in improvement in the timely initiation of nutrition therapy in patients with TBI. - *There is level 4 evidence (Musillo et al., 2018) that the utilization of multiple nutritional intervention strategies and an interdisciplinary approach to treatment may result in improvement in the timely initiation of nutrition therapy in patients with TBI.*
Other Nutritional Interventions	
Zinc Supplementation	Zinc supplementation in the immediate post-injury period may improve neurological recovery and visceral protein concentrations, but not mortality rates, in patients with ABI.

Intervention	Key Points Level of Evidence
	- *There is level 1a evidence (Khazdouz et al., 2018; Young et al., 1996) that zinc supplementation may improve neurological recovery as measured by the Glasgow Coma Scale in patients post ABI.*
Growth Hormone	Growth hormones may enhance nutritional repletion; however, the evidence is conflicting regarding improvements in nitrogen balance, in patients post ABI. - *There is level 1b evidence (Hatton et al., 2006) that patients post TBI treated with insulin-like growth factor-1/growth hormone had higher glucose concentrations and nitrogen balance compared to placebo.* - *There is level 2 evidence (Behrman et al., 1995) that growth hormone may increase serum protein, but may not be effective in improving nitrogen balance or glucose concentration in patients post head injury.* - *There is level 4 evidence (Devesa et al., 2013) that growth hormone may increase plasma IGF-1 values and improve cognitive abilities in patients post TBI.*
Increased Nitrogen Feeds	High-protein nitrogen feedings may restore nitrogen losses post ABI. - *There is level 2 evidence (Twyman, 1997) that high-protein nitrogen feedings of approximately 1 g nitrogen/90 calories may be effective for restoring nitrogen losses compared to low-protein nitrogen feedings in patients post head injury.*
Branched-Chain Amino Acids	Branched-chain amino acid supplementation may improve disability scores in individuals with ABI. - *There is level 2 evidence (from one randomized controlled trial; Aquilani et al., 2005) that branched-chain amino acid supplementation may improve disability scores compared to placebo in individuals post TBI.*
Vitamin D supplementation	Vitamin D supplement may increase GCS and GOS scores and reduce length of stay in ICU in patients with moderate to severe TBI. - *There is level 1b evidence (Sharma et al., 2020) that vitamin D supplement may increase GCS and GOS scores and reduce length of stay in ICU in patients with moderate to severe TBI.*

Introduction

After an acquired brain injury (Merimee & Rabin), a wide range of swallowing disorders may occur. Focal and diffuse cortical and brainstem damage may impair swallowing ability, leading to the development of dysphagia and aspiration (Morgan & Ward, 2001). Dysphagia can be defined as an impairment of the swallowing process (McCarty & Chao, 2021). In clinical practice, dysphagia is often described as a sensation of food or liquid stuck in the individual's chest or esophagus (Triggs & Pandolfino, 2019).

Aspiration, which may be a sequelae of dysphagia, is defined as the entry of material into the airway below the level of the true vocal cords. The two terms are not synonymous, as many individuals with dysphagia do not aspirate, although, they are closely associated (Morgan & Ward, 2001). Reported rates of aspiration post ABI vary in the literature, however, trends illustrate a decrease in the incidence of aspiration over time, particularly beyond 3-month follow-up (Kim & Suh, 2018; Morgan & Ward, 2001).

Good nutrition is critical, especially for the brain injury population. Individuals who have sustained a brain injury frequently present with feeding intolerance, and in more severe cases, require mechanical ventilation, resulting in additional challenges for the provision of adequate nutrition and the need for alternative feeding routes, such as enteral nutrition (Cook et al., 2008).

This module will discuss dysphagia, aspiration, as well as nutrition in individuals post ABI. ABI specific literature related to dysphagia, aspiration, and nutrition is limited. In 2016, a set of clinical practice guidelines for the rehabilitation of adults with moderate to severe TBI were developed by the Ontario Neurotrauma Foundation and INESSS. A portion of these guidelines focus on dysphagia and nutrition, which can be accessed here. Many of the recommendations in this section were based on the evidence found throughout that module.

Swallowing function is implicated in both dysphagia and aspiration. Swallowing has four sequential coordinated phases which are summarized in Table 4 and illustrated in Figure 1. Impairment may occur in any one of the swallowing phases, or across more than one phase. Oropharyngeal dysphagia includes the preparatory phase, oral propulsion and pharyngeal phases, while esophageal dysphagia involves the esophageal phase of swallowing (McIntosh, 2023).

TABLE 4 | The Four Phases of Normal Swallowing (Platt, 2001)

Phase	Characteristics
Oral Preparatory	Food in the oral cavity is manipulated, masticated, and mixed with saliva in preparation for swallowing. The back of the tongue controls the position of the food, preventing it from entering prematurely into the pharynx.

Oral (Propulsive)	The tongue transfers the bolus of food from anterior to posterior aspects of the oral cavity and to the pharynx, triggering the pharyngeal swallow.
Pharyngeal	Complex and coordinated movements of the tongue, pharyngeal musculature and structures propel the bolus into the esophagus, while protecting the airway.
Esophageal	Coordinated contractions of the muscles of the esophagus move the bolus through the esophagus towards the stomach.

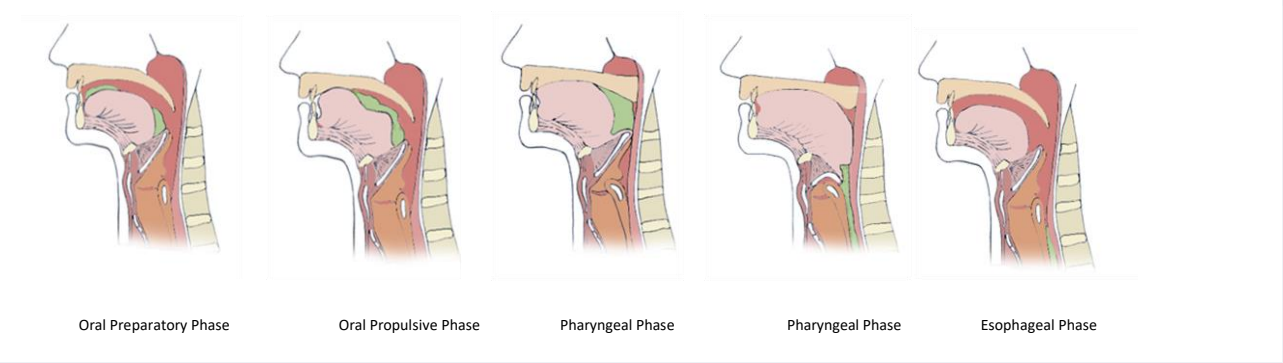


Figure 1 | Phases of Swallowing

Prevalence of Dysphagia

Dysphagia post ABI has been attributed to pharyngeal muscular dysfunction and lack of coordination, secondary to central nervous system loss of control. The reported incidence of dysphagia among individuals with brain injury varies considerably, due to differences in the timing and method of assessment, as well as the initial level of severity. Although the incidence of dysphagia can be high following ABI, swallowing function frequently improves in this population over time. Rates of dysphagia in ABI are variable, with the literature ranging between 26% and 70% (Cherney & Halper, 1996; Cherney, 1989; Field & Weiss, 1989; Halper et al., 1999; Schurr et al., 1999; Winstein, 1983). In a systematic review, Takizawa et al. (2016) found the incidence of dysphagia in traumatic brain injury to be 27% to 30%.

Many of these rates are determined at hospital admission; however, Winstein (1983) reported that at the time of discharge, 84% of those patients admitted with swallowing problems were eating orally; at follow-up, in the outpatient clinic, this number increased to 94%. The most common swallowing problems among individuals with ABI included prolonged oral transit (87.5%), delayed swallow reflex (87.5%), vallecular pooling (62.5%), and pyriform sinus pooling (62.5%) (Field & Weiss, 1989).

In a study by Mackay et al. (1999), other swallowing abnormalities included: loss of bolus control (79%), reduced lingual control (79%), decreased tongue base retraction (61%), delayed initiation of swallow (48%), reduced laryngeal closure (45%), reduced laryngeal elevation (36%), unilateral pharyngeal paralysis (24%), absent swallow reflex (6%), and cricopharyngeal dysfunction (3%). For these studies, the

most common factor impacting swallowing problems was cognitive functioning (Mackay et al., 1999; Winstein, 1983). Spontaenous jaw muscle activity has also been observed in those with an ABI at rates as high as triple as those compared to healthy controls (Kothari et al., 2018), which can result in further impairment as a result of an ABI.

Risk Factors for Dysphagia

Risk Factors for Dysphagia (Lazarus & Logemann, 1987; Mackay et al., 1999)

- Extent of brain injury
- Duration of coma
- Lower Glasgow Coma Score on admission (GCS 3-5)
- Severity of CT Scan findings
- Duration of mechanical ventilation
- Tracheostomy
- Translaryngeal (endotracheal) intubation
- Severe cognitive and cognitive-communication disorders
- Physical damage to oral, pharyngeal, laryngeal, and esophageal structures
- Oral and pharyngeal sensory difficulties

Typically, the more severe the brain injury, the more severe the swallowing issues (Logemann, 2013). However, the relationship between injury severity/characteristics and the nature of the swallowing disorder needs to be further studied. Within the literature, several studies have addressed factors that may affect the presence and severity of dysphagia post ABI (Cherney & Halper, 1996; Halper et al., 1999; Mackay et al., 1999; Morgan & Mackay, 1999). For example, injuries that result from translaryngeal intubation or tracheostomy may contribute to prolonged swallowing dysfunction in individuals with ABI (Morgan & Mackay, 1999), but their etiology is secondary compared to primary dysphagia.

Prevalence of Aspiration

When assessing an individual for signs of aspiration, a video fluoroscopic swallow study (VFSS) or, as it is also called, a modified barium swallow (MBS) study (Young et al.) may be undertaken. The VFSS, along with the fiberoptic endoscopic evaluation, have been considered to be accurate tests for objectively assessing oropharyngeal dysphagia (Giraldo-Cadavid et al., 2017). Each of these tests require the individual to swallow liquids or solids of various volumes and consistencies (from thin to thick, or thick to thin) and examines the path taken by the bolus during the swallow. This procedure allows for observation of any structural or functional anomalies as well as determining whether laryngeal penetration or aspiration occurs. Rates of aspiration within the ABI population range from 25% to 71% depending on the sample surveyed (Mackay et al., 1999; Schurr et al., 1999). Terre and Mearin (2009) followed 26 individuals with traumatic brain injury (TBI) who aspirated (35% were silent aspirators - no cough/throat clear response to aspiration), for one year. With “true” silent aspiration there are no overt signs that an individual has aspirated, and the individual themselves may not be aware that solids or liquids have entered the airway or lungs (Terre & Mearin, 2009). At 3, 6, and 12 months, the number of

individuals who aspirated steadily declined, such that aspiration was present in only 6 of the 26 individuals by the end of the first year (Terre & Mearin, 2009). For the majority of individuals, the most significant changes were seen at the 3-months post evaluation.

Regarding assessment, O'Neil-Pirozzi et al. (2003) studied 12 individuals with tracheostomy who also presented with severe disorders of consciousness and found that participants were able to complete a modified barium swallow (MBS) study successfully. In terms of potential treatment for aspiration, a study by Steele et al. (2013) found that individuals had improvements on measures of tongue pressure and reduced penetration aspiration after the completion of a 24-session tongue-pressure resistance training program. Increased tongue strength may therefore be seen as beneficial in improving swallowing and isometric tasks. Studies examining interventions for aspiration do exist in evidence-based literature, though no studies met the ERABI inclusion criteria.

Risk Factors for Aspiration

While all individuals with ABI have the potential to aspirate, there are risk factors that place individuals at higher risk (Table 5). Initial severity of the brain injury appears to be the strongest predictor of dysphagia-related aspiration. Therefore, the risk of dysphagia-related aspiration is proportional to the initial severity of head injury. Further, individuals with severe ABI, neurogenic dysphagia and a tracheostomy are at a particularly high-risk of aspiration (Morgan & Mackay, 1999). In those who require tracheostomy, the negative effects can be minimized by ensuring the use of appropriately sized tracheostomy tubes and by avoiding over-inflation of any cuff (Tolep et al., 1996).

TABLE 5 | Risk Factors for Aspiration Post ABI

Traumatic Causes	Vascular and Pathological Incidents
• Motor vehicle accidents • Falls • Assaults • Gunshot wounds • Sport Injuries **Non-traumatic Causes** • Tumours (benign/meningioma only) • Anoxia • Subarachnoid hemorrhage (non-focal) • Meningitis • Encephalitis/encephalopathy (viral, bacterial, drug, hepatic) • Subdural Hematoma	• Intracerebral hemorrhage (focal) • Cerebrovascular accident (i.e., stroke) • Vascular accidents • Malignant/metastatic tumours **Congenital and Developmental Problems** • Cerebral Palsy • Autism • Developmental delay • Down's syndrome • Spina bifida with hydrocephalus **Progressive Processes** • Alzheimer's disease • Pick's disease • Dementia • Amyotrophic Lateral Sclerosis • Multiple Sclerosis • Parkinson's disease

	• Huntington's disease

Silent Aspiration

Silent aspiration is defined as "*penetration of food below the level of the true vocal cords, without cough or any outward sign of difficulty*" (Linden & Siebens, 1983). The incidence of silent aspiration among individuals with ABI has not been well documented. One reason for this, is that aspiration cannot be diagnosed by a bedside examination, and individuals may aspirate without showing outward signs. Detailed clinical swallowing assessments have been shown to underdiagnose or miss cases of aspiration (Splaingard et al., 1988). Silent aspiration may be missed in the absence of an instrumental assessment, such as a modified barium swallow (MBS) study or fiberoptic endoscopic examination of swallowing (FEES). Silent aspiration should be suspected in individuals with ABI who have recurrent lower respiratory infections, chronic congestion, low-grade fever, or leukocytosis (Muller-Lissner et al., 1982). Clinical markers of silent aspiration may include a weak voice or cough, or a wet-hoarse vocal quality after swallowing. Lazarus and Logemann (1987) identified aspiration in 38% of their ABI sample and found that many of these individuals, despite aspirating, did not produce a reflexive cough and required prompting to clear aspirated material.

Pneumonia & Aspiration

Aspiration is a significant challenge for clinicians caring for individuals with TBI. Aspiration may lead to aspiration pneumonia, an infectious process that may be acquired from the inhalation of gastric contents or from food/liquid/oral bacteria entering the airway from above. Both of these events often result in greater rates of morbidity and mortality, as well as longer rehabilitation stays and discharge to long-term care facilities (Shiferaw et al., 2022). Aspiration pneumonia is often related to swallowing difficulties (e.g., dysphagia), particularly in individuals who present with an ineffective cough reflex, those with disorders of consciousness or in the context of a neurological disease such as Multiple Sclerosis and Parkinson's Disease (Mandell & Niederman, 2019). Additional risk factors for aspiration pneumonia include tube feeding, infrequent ambulation, mechanical ventilation, and poor dentition in older adults (Niederman & Cilloniz, 2022).

Following severe TBI, predictors of pneumonia may include dependence in self-feeding and oral care, the amount of tooth decay, the need for tube feeding, greater than one medical diagnosis, smoking, and the total number of medications (Langmore et al., 1998). In a study by Vejdan and Khosravi (2013), individuals who received flexible bronchoscopy and bronchoalveolar lavage in combination with routine

methods had fewer incidences of nosocomial pneumonia when compared to routine clearance procedures alone (14% versus 34%,), demonstrating that it is possible to treat aspiration.

The clinical criteria used to define aspiration pneumonia varies between studies, impact the reported incidence. Due to the absence of ABI specific studies, the criteria used within the stroke literature is provided in Table 6.

TABLE 6 | Criteria for Defining Aspiration Pneumonia in Stroke

Author/ Year Country	Criteria
Dziewas et al. (2008) Germany	Pneumonia was diagnosed on the basis of 3 of the following indicators: temp >38°C, productive cough with purulent sputum, abnormal respiratory exam including tachypnea, (>22 breaths/min), tachycardia, inspiratory crackles, bronchial breathing, abnormal chest x-ray, arterial hypoxemia (PO2 <9.3 kPa) and a positive gram stain.
Carnaby et al. (2006) USA; Dziewas et al. (2004) Germany	Three of the following indicators: temp >38°C, productive cough with purulent sputum, abnormal respiratory exam including tachypnea, (>22 breaths/min), tachycardia, inspiratory crackles, bronchial breathing, abnormal chest x-ray, arterial hypoxemia (PO^2 <9.3 kPa) and positive chest radiography.
Teasell et al. (1996) Canada	Radiological evidence of consolidation, and at least one other clinical feature including granulocytosis, temp >38°C and/or shortness of breath.
Smithard et al. (1996) UK	Presence of at least two of the following: tachypnea (>22/min), tachycardia, aspiratory crackles, bronchial breathing, or antibiotic usage.
Kidd et al. (1995) UK	Production of sputum in conjunction with the development of crackles on auscultation, with or without the presence of fever or leucocytosis.
DePippo et al. (1994); Holas et al. (1994) USA	A positive chest x-ray or the presence of at least three of the following: temp >100 °F, drop in PO^2 >10 torr, presence of WBC in sputum and/or positive sputum culture for pathogen.
Johnson et al. (1993) USA	Segmental consolidation or infiltrate on chest x-ray or clinical diagnosis which included an episode of respiratory difficulty with segmental moist rales on auscultation and two other symptoms including temp >100 °F, WBC >10,000 or hypoxia.

Within the TBI population, there are significant gaps in the literature in this area, and the literature mostly focused on ventilator-associated pneumonia rather than aspiration pneumonia in TBI population (Hui et al., 2013; Jovanovic et al., 2015; Plurad et al., 2013); thus, we rely on data from stroke populations to infer an understanding of the relationship between dysphagia, aspiration, and aspiration pneumonia. In stroke, an association between pneumonia and dysphagia/aspiration has been reasonably well-established, in that the presence of dysphagia and aspiration has been associated with an increased risk of pneumonia (Dziewas et al., 2004).

A cohort study of 2545 individuals with severe brain injury showed an in-hospital aspiration pneumonia rate of 3.6%. Individuals with TBI were 79 times more likely to die from aspiration pneumonia than the general population after discharge. Risks were higher for individuals discharged to a nursing home, those with severe ongoing functional disability, dysphagia at discharge, and those who had experienced in-hospital aspiration pneumonia or required PEG insertion (Howle et al., 2011). Hansen et

al. (2008) explored the risk factors associated with pneumonia in individuals with severe TBI and found that pneumonia was more common among individuals with low levels of consciousness and for those with a feeding or tracheotomy tube, similar to the patterns seen in stroke. Glasgow Coma Scale (GCS) scores and Rancho Los Amigos scale scores were also associated with pneumonia rates in individuals who had lower GCS scores, as well as individuals with lower Rancho Los Amigo Scale scores had increased risk of aspiration pneumonia. Additionally, these two scales, along with the Functional Oral Intake Scale and Functional Independence Measure (Muller-Lissner et al., 1982) were found to be predictive of rates of return to an unrestricted diet (Hansen et al., 2008). Further, Hui et al. (2013) found that individuals were more likely to develop pneumonia if they were older, on ventilation for a longer period of time, suffered blunt trauma, and/or had suffered a severe TBI. Similarly, a prospective cohort study of 144 people with TBI under mechanical ventilation, showed the severity of TBI and age influenced the development of late ventilator-associated pneumonia (Jovanovic et al., 2015).

Dysphagia Assessment

Following a head injury, a thorough assessment of swallowing is often required. Assessments may include a bedside clinical evaluation and/or a radiological procedure such as the MBS/video fluoroscopic swallow study, or a FEES most often completed by a Speech-Language Pathologist (SLP). Assessments should be completed at various times throughout rehabilitation admissions. Cognitive-communication impairments, physical deficits, hydration, nutritional needs, and risk factors for swallowing difficulties must be considered when making dietary decisions. Once again, there are limited studies discussing assessment of dysphagia post ABI specifically; therefore, the stroke models of care will be highlighted.

To be clinically useful, screening tests need to be valid, reliable, easy to use, non-invasive, quick to administer (15-20 min), and pose little risk to individuals. Although many screening tools have been developed it is unclear how many of them are used in institutions beyond those where they were initially developed. Many institutions use informal processes, or simply restrict all food and drink intake until an assessment has been completed by a Speech Language Pathologist (SLP).

Although ERABI focuses primarily on interventional studies, information pertaining to assessment tools used in dysphagia practice have been included within this section to increase its clinical utility. Despite being commonly used in practice with ABI populations, none of these tools have been studied extensively within this population.

Bedside Clinical Examination

Several forms of clinical or bedside swallowing evaluations (BSE) have been described for the purposes of screening and/or assessment. Some of these methods target specific functions or tasks, while others evaluate swallowing ability using a more comprehensive approach (Table 7). The clinical BSE typically

involves general observations, an oral motor examination, a review of expressive language, receptive ability to understand directions, and a review of current medications (Halper et al., 1999). The protocol may or may not include a water-swallowing test (WST), and in some cases various consistencies of food and liquids are trialled. While the BSE is non-invasive and easy to perform, this method has been shown to poorly predict the presence of silent aspiration. Moreover, aspiration cannot be distinguished from laryngeal penetration using a bedside evaluation, resulting in the over diagnosis of observed aspiration and, in some cases, needless dietary restrictions (Smith et al., 2000).

The BSE is typically completed by an SLP or a professional trained in dysphagia. This examination is generally completed once the patient's history has been reviewed by the clinician (Logemann, 1989). Clinicians are expected to make several observations: status of lip closure, oral versus nasal breathing, management of secretions, patient's awareness of secretions, patient's awareness of clinician's approach, and the overall cognitive and communication presentation of the patient (Logemann, 1989).

TABLE 7 | Aspects Included in Various Bedside Screening/Assessment Tools for Dysphagia

Author/Year	Components of Selected Dysphagia Screening/Assessment Tools	
Westergren et al., (2001) (Screening for eating difficulties)	• Ingestion: sitting position, manipulation of food on plate, transport of food to mouth	• Deglutition: opening or closing of mouth, manipulating food in the mouth
Perry (2001) (Screening)	• Consciousness level • Trunk control while seated • Volitional cough • Control of saliva	• Tongue control • Ease of breathing • Voice quality • Includes water-swallowing test
Mann et al., (2000) (Assessment)	• General examination: Consciousness, cooperation, language function, verbal/oral praxis, articulation • Oral preparation: Control of saliva, lip seal, tongue movement/strength, oral preparation, assessment of respiration	• Oral phase: Gag reflex, palatal movement, oral transit time, bolus clearance, water swallowing test • Pharyngeal phase: Pharyngeal control/pooling, laryngeal elevation, reflex/voluntary cough, voice quality
Daniels et al. (1997) (Screening)	• Assessment of mandible, lips, tongue, velum • Gag Reflex • Cough or voice change with swallow • Facial numbness/tingling	• Dysphonia • Dysarthria • Volitional cough • Includes water-swallowing test
Smithard et al., (1996) (Screening)	• Consciousness level • Head and trunk control • Breathing pattern • Lip closure • Palate movement	• Laryngeal function • Gag reflex • Voluntary cough • Includes water-swallow test
DePippo et al., (1992) (The Burke Dysphagia Screening test)	• Bilateral/brainstem stroke • History of pneumonia • Cough with feeding/3 oz. water	• Failure to finish ½ of meals • Prolonged time required for feeding • Presently fed non-orally

Water Swallowing Test

The WST originally required an individual to swallow 3oz (90mL) of water, however, smaller amounts have also been used. Although the WST has not been studied in individuals with ABI, it warrants inclusion given its persistent use by health providers (especially non-SLPs) at the bedside. This sensitivity and specificity of this test has been studied extensively within the stroke population.

Stroke populations are used to illustrate the benefit of these screening tools, as research and supporting evidence specific to the TBI population is lacking. In a systematic review that evaluated the accuracy of 49 individual clinical screening tests for oropharyngeal dysphagia, Martino et al. (2000) suggested that there was only sufficient evidence to support the value of two tests: abnormal pharyngeal sensation and the 50 mL WST. Both tests assessed only for the presence or absence of aspiration. Their associated likelihood ratios were 5.7 (95% CI 2.5-12.9) and 2.5 (95% CI 1.7-3.7), respectively. Evidence suggests that the number of aspirations observed increases as the amount of liquid increases (Osawa et al., 2013). Daniels et al. (2012) reviewed the sensitivity, specificity, and positive likelihood ratio of items on 17 screening tools designed to detect aspiration. Items with high sensitivity (>80%) included weak palatal movement, cough on a 50 mL and repeated 5 mL WST, dysarthria, abnormal volitional cough, abnormal voice, and abnormal pharyngeal sensation. Only 1 item (impaired pharyngeal response) was associated with a likelihood ratio greater than 10, the clinically relevant threshold. According to Nishiwaki et al. (2005), cough/voice change in the WST was the only variable that was significantly associated with aspiration on modified barium swallow (VMBS) examination, with a sensitivity of 72% and a specificity of 67%.

Video fluoroscopic Modified Barium Swallow Studies

When aspiration is suspected, the Video fluoroscopic Modified Barium Swallow (VMBS) study, often shortened to a Modified Barium Swallow (MBS) study, is considered to be the “gold standard” in confirming the diagnosis (Splaingard et al., 1988). A MBS study examines the oral preparatory and pharyngeal phases of swallowing; however, an individual must have sufficient cognitive and physical skills to undergo testing (Bach et al., 1989). Typically, the individual is placed in a seated position, in a chair designed to simulate the ideal/optimal mealtime posture. Radio-opaque materials of various consistencies are tested: barium impregnated thin and thick liquids, pudding, bread, and cookies are routinely used. Various aspects of the oral preparation, laryngeal, and pharyngeal involvement are noted during the radiographic examination (Table 8). In some, but not all cases, it may be appropriate to follow the MBS study with a chest x-ray to document any barium, which may have been aspirated into the tracheobronchial tree. If a MBS study is indicated and impairments are found, a second MBS study may be appropriate in 1 to 3 months, if swallowing concerns persist and to assist in care planning.

Those who aspirate over 10% of the test bolus or who have severe oral and/or pharyngeal motility problems on MBS testing are considered at high risk for pneumonia (Logemann, 1983; Milazzo et al., 1989). In many cases, it is difficult to practically assess whether 10% or more of the test bolus has been aspirated, particularly since images are seen two dimensionally. Nevertheless, the degree of aspiration seen on MBS study is a critical observation in this study. Predicting whether an individual will develop pneumonia in the context of aspiration is dependent on many factors as discussed earlier, including poor oral health, having a compromised immune system and the overall cognitive, communicative and physical health of the individual with ABI.

While the MBS study can confirm the presence and extent of aspiration, it more importantly reveals the mechanism of the swallowing disorder and allows the clinician the opportunity to explore various approaches to management. Aspiration most often results from a functional disturbance in the pharyngeal phase of swallowing related to timing, reduced laryngeal closure or reduced pharyngeal constriction. An MBS study is recommended in those cases where the individual is experiencing obvious problems maintaining adequate hydration/nutrition, where concern is expressed regarding frequent choking while eating, or in the case of recurrent respiratory infections. Other factors such as cognition, cognitive-communication, depression, underlying lung disease, and being immunocompromised must also be considered.

TABLE 8| Radiological Evaluation during VMBS (Bach et al., 1989)

Phase of Swallowing	Structure Evaluated within Phase	Function Evaluated within Phase
Oral Phase	Lips	Closure
	Tongue	Anterior and posterior motion with consonants; motion and coordination during transport, and manipulation of the bolus
	Soft Palate	Evaluation and retraction with consonants
	Jaw	Motion
	Oral	Pocketing
Pharyngeal Phase	Swallow	Delay, absence
	Peristalsis or pharyngeal stripping/constriction	Residue in valleculae, pyriform sinuses, nasopharyngeal regurgitation
Laryngeal Phase	Elevation of larynx	
	Penetration into laryngeal vestibule	
	Aspiration	

Phase of Swallowing	Structure Evaluated within Phase	Function Evaluated within Phase
	Cough	Presence, delay, effectiveness/productiveness of cough
	Vocal cord function	
Post Exam Chest X-Ray	Chronic Stages	
	Presence of barium in valleculae, pyriform sinuses, tracheobronchial tree, lungs	

Fiberoptic Endoscopic Evaluation of Swallowing (FEES)

Although MBS (or VMBS) studies are considered by some to be the gold standard for detection of aspiration, other clinical assessment techniques are currently used as they are more cost effective, more easily accessed, or easier to administer. FEES is recognized as an objective tool for the assessment of swallowing function and aspiration. FEES is a procedure that allows direct viewing of swallowing function by passing a very thin flexible fiberoptic tube through the nose to view the path through the pharynx during swallowing. FEES allows for the full evaluation of the swallow function as food passes from the mouth into the pharynx. The evaluation identifies functional abnormalities and helps to determine the safest position and food texture for the individual to maximize hydration/nutritional status and to reduce or eliminate the risk of aspiration and unsafe swallowing. In addition to assessing the motor components of swallowing, FEES can also include a sensory testing assessment when an air pulse is delivered to the mucosa innervated by the superior laryngeal nerve. This form of assessment is known as flexible endoscopic examination of swallowing with sensory testing.

As a result of the multiple benefits of FEES (reliability, safety, ease of administration, low cost, and lack of exposure to radiation), this tool has gained much support for the detection and management of dysphagia, particularly in acute stroke (Bax et al., 2014). FEES in combination with a cough reflex test and clinical swallowing evaluation may improve criteria for inclusion of best candidates for FEES, making this service more efficient and productive. The selection of individuals for referral to instrumental assessment may be improved by the use of these assessments together as they provide stronger evidence for the presence of dysphagia and subsequent complications among those who fail the cough reflex test (Bax et al., 2014). This is important, as conflicting evidence from other studies suggests that increased hospital length of stay (LOS) is associated with increased rates of pneumonia (Finlayson et al., 2011; Wilson & Howe, 2012), while work by Bax et al. (2014) suggested the opposite to be true. The authors explained that the relationship between LOS and rates of pneumonia may be due to the availability of FEES which actually leads to a higher referral rate for swallowing rehabilitation and a subsequent increase in length of stay. Most importantly, as an outcome measure however, there was an

increase in the proportion of individuals who left the hospital on regular diets. Overall, the use of FEES, especially in combination with cough reflex testing, appears to benefit patient health outcomes.

A good quality randomized controlled trial (RCT) assessed the use of Facial-Oral Tract Therapy versus FEES as a standard assessment indicating the opportunity for initiation of oral feeding (Kjaersgaard et al., 2014). After excluding participants who developed pneumonia outside of the primary study criteria, there was no difference in the incidence of this respiratory infection between the two groups (3/62 Facial-Oral Tract Therapy participants; 4 of 57 FEES participants). These results were supported in a study by Barquist et al. (2001), who found that the risk of pneumonia was not significantly different between 70 participants screened with either FEES or clinical assessment, within 48 hours of endotracheal intubation. It seems that FEES, when combined, may be beneficial to some clinical non-instrumental assessments such as Facial-Oral Tract Therapy in reducing the risk of aspiration pneumonia after initiating oral feeding.

Aviv (2000) compared the incidence of pneumonia over a one-year period between participants screened by MBS or FEES for dysphagia and aspiration with sensory testing and treated based on their respective outcomes. For individuals with stroke, the incidence of pneumonia for those assessed with FEES with sensory testing was significantly lower compared to those assessed with MBS. The authors speculated that one of the reasons for the lower incidence might be due to the sensory testing component of the FEES examination, absent from the MBS evaluation, which was used to guide management more effectively.

Rather than attempt to compare the accuracy of swallowing abnormalities assessed between VMBS and FEES evaluations, Leder and Espinosa (2002) compared the utility of six clinical identifiers of aspiration (dysphonia, dysarthria, abnormal gag reflex, abnormal volitional cough, cough after swallow, and voice change after swallow) with FEES assessment to determine the accuracy of predicting aspiration risk following stroke. Their results suggest that the ability to correctly identify individuals not at risk of aspiration was poor using clinical criteria (low specificity). However, two studies conclude that FEES is the gold standard to assess the accuracy along with either the WST and/or pulse oximetry to detect aspiration within the stroke population (Chong et al., 2003; Lim et al., 2001).

Pulse Oximetry

Pulse oximetry has also been suggested as a method of detecting aspiration, based on the principle that aspiration of food into the airway leads to bronchospasm or airway obstruction, which leads to a reduction in oxygen saturation. This technique is non-invasive, requires little patient cooperation and is easy to obtain, however, its accuracy in detecting aspiration is unproven and it remains uncertain whether oxygen desaturation can predict aspiration. Wang et al. (2005) reported no significant association between the reduction in oxygen saturation and aspiration, identified simultaneously by

MBS, among 60 participants with dysphagia due to stroke and nasopharyngeal cancer. While Collins and Bakheit (1997) reported that pulse oximetry could be used to detect a high proportion of individuals with stroke who aspirated, or did not, during the MBS study (81.5%).

Although use of pulse oximetry would be a quick and non-invasive method to detect aspiration following stroke, the association of aspiration with oxygen desaturation has been inconclusive. Generally, its performance when measured against MBS studies has been poor due to its low sensitivity and specificity (39%-87%) (Collins & Bakheit, 1997; Smith et al., 2000; Wang et al., 2005). Therefore, it is unclear whether it is a clinically viable tool for the detection of dysphagia and aspiration.

Blue Dye Assessment for Swallowing

The blue dye assessment for swallowing has been used since the early 1970's with individuals who have a tracheostomy, however, the accuracy of the test has been questioned since the 1980's (O'Neil-Pirozzi, Lisiecki, et al., 2003). For people with a tracheostomy, this assessment involves placing blue dye on the tongue or, in the case of the modified blue dye test, mixing it with water or semisolid food. If blue dye appears in or around the tracheostomy tube, or at defined intervals during suctioning, then the individual is suspected to have aspirated. This test tends to be relatively easy to administer, inexpensive and can be performed at a patient's bedside. Unfortunately, research has shown that the test may have a 50% false-negative error rate in the detection of aspirated material (Belafsky et al., 2003; Brady et al., 1999; Donzelli et al., 2001). There is conflicting evidence regarding both the sensitivity and specificity of the blue dye assessment in specific population groups as well. Belafsky et al. (2003), in a study of 30 participants with tracheostomies, concluded that the use of the modified Evans blue dye test (MEBD) is beneficial specifically in individuals who have a tracheostomy tube (82% sensitivity) and particularly those who receive mechanical ventilation (100% sensitivity). O'Neil-Pirozzi, Momose, et al. (2003), found that the blue dye test was unable to correctly identify aspiration in 20% of the study participants with tracheostomy and 38% of participants with a tracheostomy who were not aspirating.

Brady et al. (1999), in a study looking at the effectiveness of the MEBD test and the MBS, found that the MEBD test was not able to detect "trace amounts" of aspiration in participants who had a tracheostomy. On the other hand, if participants aspirated more than "trace amounts", then the MEBD was able to detect it. The authors recommended that the MEBD be followed by a MBS to rule out the possibility of trace aspiration. (Brady et al., 1999) Although this test is used in practice with individuals post ABI, no studies were found looking at its effectiveness within that specific population, therefore, individuals who are assessed for aspiration or dysphagia using the MEBD test should be followed up with a more established test with greater sensitivity and specificity like the MBS study or FEES.

Additional Methods

In addition to conventional assessment methods, tracheal pH monitoring has been used experimentally to detect drops in pH, which may indicate aspiration. Clayton et al. (2006) reported that in 9 of 32 participants examined, there was a drop in tracheal pH following ingestion of acidic foods. Tracheal pH was monitored using a sensor, which was inserted into the trachea by the cricothyroid membrane. All participants were studied following the ingestion of foods which had been considered safe on the basis of a MBS examination.

Another assessment tool is voice analysis. Ryu et al. (2004) evaluated voice analysis to clinically predict laryngeal penetration among 93 participants (46% of whom had suffered a stroke) using MBS study to confirm aspiration. Of five voice parameters tested (average fundamental frequency, relative average perturbation, shimmer percentage, noise-to-harmonic ratio, and voice turbulence index), changes in relative average perturbation most accurately predicted aspiration.

Cervical auscultation, another tool to assess aspiration, is conducted using a stethoscope or other listening device (Borr et al., 2007; Leslie et al., 2007; Youmans & Stierwalt, 2005). It is believed that this type of test can provide additional information on the pharyngeal swallow in all participants without any additional costs or intrusive methods (Borr et al., 2007; Youmans & Stierwalt, 2005). Cervical auscultation was compared to the VMBS in participants being treated for dysphagia (Zenner et al., 1995). Although agreement was found between the two tests on the oral phase, pharyngeal phase, and diet management components, the VMBS did appear to be slightly more sensitive in identifying individuals who had aspirated. In another study, Stroud et al. (2002) found that raters were able to identify individuals who were aspirating quite easily but challenges arose when evaluating patients who were not aspirating, resulting in a significant number of false positives. Due to the limited evidence for cervical auscultation, caution should be taken when using this technique and it should not be used in isolation (Leslie et al., 2007).

Management of Dysphagia

The management of dysphagia is critical in individuals with brain injury, as dysphagia may lead to dehydration, malnutrition, and prolonged hospital stays, especially if the individual develops aspiration pneumonia (Eskildsen et al., 2021). For individuals with dysphagia following head injury, based on the status of swallowing function at the time of admission, three distinct types of rehabilitation programs have been described: 1) non-feeding, 2) facilitation and feeding, and 3) progressive feeding. Given that individuals with dysphagia who are fed by someone else have a 20 times greater risk of pneumonia than those who are able to feed themselves (Langmore et al., 1998), rehabilitation of dysphagia often aims to help individuals become independent in their feeding skills, and to improve safety and care outcomes.

The non-feeding program was designed as a stimulation program for very low-level individuals, to prepare them for later feeding. It includes desensitization techniques (e.g., stroking, applying pressure, or stretching) to facilitate normal swallowing, sucking, and intraoral responses (Winstein, 1983). The

facilitation and feeding program use small amounts of puree consistency food to promote normal feeding patterns (Winstein, 1983). Finally, the progressive feeding program uses specialized techniques to help the individual develop swallowing endurance by systematically increasing the amount of oral intake. This progressive feeding program continues until the individual can consume a complete meal within thirty minutes without difficulty (Winstein, 1983).

For individuals who are safe with some form of oral intake, therapeutic strategies utilized in dysphagia management can be divided into two categories: (a) compensatory treatment techniques and (b) therapy techniques (Logemann, 1999). Compensatory treatment techniques do not involve direct treatment of the swallowing disorder, rather they reduce or eliminate the symptoms of dysphagia and risk of aspiration by altering how swallowing occurs (Logemann, 1991, 1999). The types of compensatory strategies include: (a) postural adjustment of the head, neck, and body to modify the dimensions of the pharynx and improve the flow of the bolus, (b) sensory stimulation techniques used to improve sensory input either prior to or during the swallow, (c) food consistency and viscosity alterations, (d) modifying the volume and rate of food/fluid presentation, and (e) use of intraoral prosthetics (Logemann, 1999). Conversely, therapy techniques are designed to alter the swallow physiology (Logemann, 1999). They include range-of-motion and bolus handling tasks to improve neuromuscular control without actually swallowing. They also include swallowing maneuvers that target specific aspects of the pharyngeal stage of the swallow. Medical and surgical management techniques are included in this category (Logemann, 1999), with these interventions typically only introduced once trials with more traditional behavioural treatment techniques have proven to be unsuccessful.

Several interventions have been investigated for the treatment of dysphagia. Included among these are vocal fold adduction exercises, range of motion exercises for the lips, tongue, and jaw, and chewing exercises (Logemann, 1993). Many of these exercises, although tested within stroke or other populations, have not been tested specifically within the ABI population. As there is a need for more clinical data supporting dysphagia treatments within an ABI population, this section will focus on research based on both ABI populations that did not meeting inclusion criteria, as well as stroke patient data and will discuss the literature supporting dysphagia management in a stroke population.

Oral Motor Exercises

Exercises introduced to those who have developed a swallowing disorder include various oral motor exercises, including range of motion exercises for the tongue and the pharyngeal structures (Logemann, 1998). These exercises are designed to improve strength, movement, awareness, and muscle coordination when swallowing (Kramer et al., 2007). To aid in the improvement of oral transit, exercises to assist in tongue elevation and lateralization may be recommended. Here the individual may be asked to perform very specific tongue exercises in an effort to improve speech and swallowing (Logemann, 1998). Individuals may also be asked to participate in tongue resistance exercises (pushing the tongue

against a tongue blade or popsicle stick for 1 second) and bolus control exercises (to allow the individual to learn to control or manipulate items placed in the mouth) (Logemann, 1998).

Range of Motion Exercises

When participating in range of motion exercises, the individual is asked to bear down while holding their breath from a seated position. This exercise is not recommended for those with uncontrolled blood pressure (Logemann, 1998). It is recommended that this exercise be done 5 to 10 times each day for 5 minutes.

Vocal Fold Adduction Exercises

Vocal fold adduction exercises aim to improve vocal quality and reduce the risk of aspiration. Individuals are asked to bear down, with one hand against a chair while producing a clear voice. This is done five times. The individual is then asked to repeat an "ah" sound five times. Again, it is recommended that these exercises be repeated three times in sequence, 5 to 10 times each day for five minutes. If there is no significant improvement in swallowing at the end of one week, individuals may be asked to pull up on the seat of a chair, while sitting in it, and prolong phonation (Logemann, 1998). This exercise is recommended for those individuals whose vocal folds fail to close completely (Kramer et al., 2007).

Strengthening Exercises

Exercises which strengthen the muscles in the throat and neck may improve swallowing function. However, individuals need to be able to physically complete the required motions without injury to use this treatment method (Kraaijenga et al., 2015).

The Shaker Exercise

For the Shaker exercise, individuals are asked to lay flat on the floor or in bed and raise their heads high enough to see their toes. This position is held for one minute, the person then rests for one minute. The exercise is repeated three times. Following this sequence, the individual lifts their head, looks at their toes, and then lowers their head. This head up then down sequence is repeated 30 times. It is recommended that the Shaker exercise be completed three times per day for a period of six weeks. This exercise has been shown to have some success in improving hyolaryngeal movement (Logemann, 1998; Shaker et al., 2002; Shaker et al., 1997); however, it has not been studied specifically in the ABI population.

Chin Tuck Against Resistance

An alternative exercise to strengthen suprahyoid muscles is the chin tuck against resistance exercise. This involves two steps for participants: 1) squeezing a rubber ball by tucking the chin in for 10s (isometric) and 2) squeezing a rubber ball with the chin as hard as possible 10 consecutive times (isokinetic) (Yoon et al., 2014). A preliminary study that included healthy participants evaluating the

potential use of the chin tuck against resistance exercise in populations with dysphagia concluded that this method resulted in greater maximum surface electromyography when compared to the Shaker exercise (Yoon et al., 2014). However, in order to determine the effectiveness of exercising suprahyoid muscles for dysphagia the authors stated that clinical trials are needed (Sze et al., 2016; Yoon et al., 2014).

Swallow Maneuvers

During the acute stage of recovery, individuals may experience more swallowing difficulties than they do during later rehabilitation. Failing to address and treat swallowing difficulties in the early stages may lead to compliance issues with the recommended diets, and possible setbacks secondary to aspiration pneumonia. Overall, this can hinder the person's ability to participate in formal rehabilitation. Post-ABI swallowing difficulties are often the result of eating too quickly, taking large bites, cognitive impairments, and decreased swallowing sensitivity (Logemann, 1998). Swallowing difficulties may be addressed through four maneuvers traditionally, but they require the patient to follow directions, be alert, and be able to exert the physical effort it takes to perform the maneuvers correctly (Kramer et al., 2007).

Supraglottic Swallow

This maneuver is meant to close the airway at the level of the true vocal folds before and during the swallow, as well as clear residue afterwards (Logemann, 1997; Logemann, 1998). Individuals are asked to hold their breath while swallowing and then to cough immediately after the swallow. This maneuver encourages closure of the true vocal cords to address reduced or delayed vocal fold closure or delayed pharyngeal swallow. The cough portion of this maneuver is meant to eject any objects or residue within the laryngeal vestibule.

Super-Supraglottic Swallow

This maneuver targets closure of the entrance to the airway both before and during the swallow, increases pressure generation, and aims to clear residue after the swallow is complete (Logemann, 1998). During this maneuver the individual completes the following sequence: 1) take a deep breath, 2) hold the breath while bearing down hard, 3) swallow hard while holding this breath, 4) cough immediately after the swallow and clear throat, and 5) swallow again (Logemann et al., 1997).

Effortful Swallow

Effortful swallow is meant to increase posterior movement of the tongue base (Kramer et al., 2007). This technique involves asking the individual, as they swallow, to squeeze hard with all the muscles they use for swallowing (throat and neck muscles).

Mendelsohn Maneuver

The objective of this maneuver is to address decreased laryngeal movement and discoordination of the swallow. Improvements in swallowing function are achieved through increasing the extent and duration of laryngeal elevation which increases the duration and width of the cricopharyngeal opening (Logemann, 1998). Typically, individuals are asked to swallow, but as they do so, to hold their larynx (i.e., Adam's apple) elevated for two to three seconds prior to completing the swallow.

Thermal-Tactile Stimulation

Thermal stimulation or thermal-tactile stimulation was developed to stimulate the swallowing reflex in individuals who have neurological impairment (Lazzara et al., 1986). The procedure for thermal-tactile stimulation involves having the person open their mouth and applying a cold laryngeal mirror to the base of the faucial arches. The mirror, while being in contact with the arch, is rubbed up and down five times. For individuals who have sustained a trauma, contact will be made on the normal (non-injured) side of the mouth (Logemann, 1998). Pharyngeal swallow may not be triggered at the time of stimulation, but the purpose is to heighten the sensitivity for swallowing via the central nervous system. It is hoped that once the person attempts to swallow, the pharyngeal swallow will be triggered more quickly (Logemann, 1998).

The use of a chilled laryngeal mirror applied to the anterior faucial pillars (three strokes per side) before swallowing was compared to 10 consecutive swallows of semi-solid boluses in 22 participants with dysphagia post stroke (Rosenbek et al., 1996). Following the stimulation, participants were asked to swallow a bolus. Results indicated that the duration of stage transition and total swallow duration was reduced following thermal stimulation (Rosenbek et al., 1996). Similar to the use of oral motor exercises included earlier, this method requires further research before conclusions on its efficacy in post-ABI populations may be made.

Postural Techniques

Physically moving the person to change the position of the head, neck, and/or body may assist in changing the direction of the bolus flow, thereby improving pharyngeal clearance and/or reducing the risk of aspiration. Five postures that have been shown to have some success in assisting individuals improve their swallowing function are presented in Table 9 below (Logemann, 2008).

For individuals with significant cognitive deficits post injury, having the person engage in any one of these techniques may be challenging. Generally, it has been suggested that individuals with oral and pharyngeal deficits consistently do the following: remain upright for 30 minutes post meal to reduce the risk of aspiration, take controlled bites/sips, alternate solids and liquids, take multiple swallows, and clear or remove food that has pocketed in the mouth (Kramer et al., 2007).

TABLE 9 | Five Postures to Improve Swallowing Function (Logemann, 2008)

Postural Change	Impact on Swallowing Functions
1. Chin Down Posture	• May be helpful for those who have tongue base retraction issues – potential benefit should be confirmed on instrumental assessment. • Mechanism of change widens the valleculae, allowing the valleculae to contain the bolus in event of pharyngeal delay.
2. Chin Up Posture	• May be helpful for those who have oral tongue propulsion problems – potential benefit should be confirmed on instrumental assessment. • Aids in gaining adequate lingual pressure to drive the food or liquid out of the mouth and into the pharynx.
3. Head Turn (left or right)	• Involves rotating the head to the side that is damaged. • Bolus is then directed through the "normal" safe side.
4. Head Tilt (left or right)	• Head is tilted toward the stronger side, to promote the flow of food and liquid through that side.
5. Lying Down	• Effective in those with posterior pharyngeal wall contraction or reduced laryngeal elevation with resulting residue and subsequent aspiration after swallowing – potential benefit should be confirmed on instrumental assessment. • Residual or pooling of food or liquid in the pharynx is less able to enter the airway as gravity pulls the bolus towards the posterior pharyngeal wall and in more easily moved through to the esophagus (Drake et al., 1997; Rasley et al., 1993).

Diet Modification

Modification in consistency and viscosity of foods and liquids is common practice in the management and treatment of dysphagia (Melotte et al., 2020). Unfortunately, standardization of these diets, as well as the language used to describe them has been challenging. Although an attempt has been made to standardize dysphagic diets (McCallum, 2003), there continued to be significant variability in their use in clinical practice, and how diets for dysphagia were labelled. The following table illustrates examples of diets for dysphagia (Table 10). These examples illustrate the wide variability in description and detail in diets for those with dysphagia.

It should be noted that restrictions to diet and specific consistencies of food should be the last strategy examined (Logemann, 1997). Restrictions to diets and consistencies, especially thin fluids, can be very challenging for individuals (Logemann, 1997). Often patients begin with a very restrictive diet (liquids of various consistencies – purees) and move to less restrictive diets (diced to regular foods) at a pace that is determined to be safest for that individual (Kramer et al., 2007). Asking the person to limit the amount of food they attempt to swallow (taking smaller bites) will also help reduce difficulties with swallowing.

International Dysphagia Diet Standardization Initiative

In 2013, an International Dysphagia Diet Standardization Initiative (IDDSI) committee was formed from a volunteer group of individuals in nutrition & dietetics, medicine, speech-language pathology, occupational therapy, nursing, patient safety, engineering, food science & technology. The goal was to

develop standardization in terminology used in describing dysphagia diets for individuals across age, care settings and cultures, internationally. The work by this committee resulted in the creation of what is now known as the International Dysphagia Diet Framework (2018).

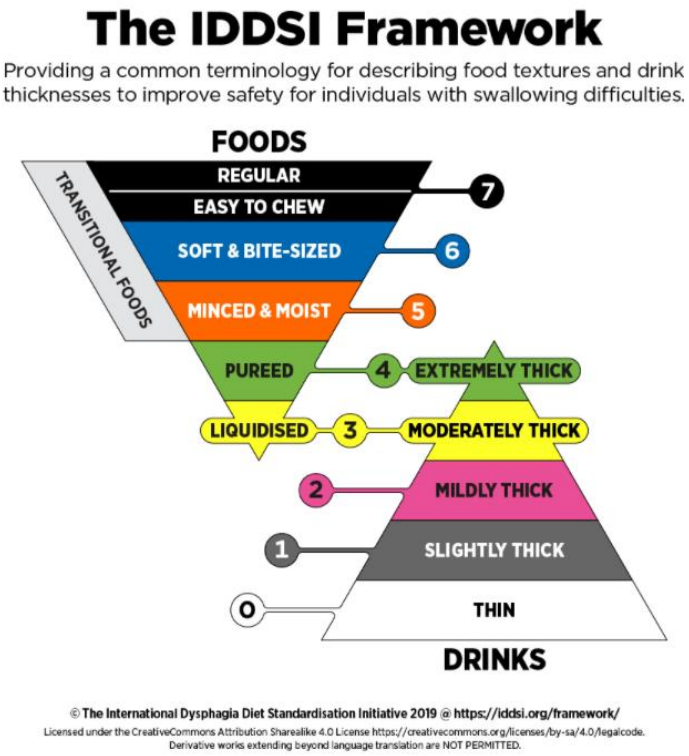
Research efforts by Steele et al. (2018) to evaluate the International Dysphagia Diet Standardization Initiative Functional Diet Scale showed strong consensual validity, criterion validity, and interrater reliability. In their study, 176 respondents from 29 countries completed a web-based survey related to 16 clinical cases. They found poorest consensus with the cases "involving liquid-only diets, transition from non-oral feeding, or trial diet advances in therapy". Perhaps more telling was the finding that "most (>70%) respondents indicated enthusiasm for implementing the International Dysphagia Diet Standardization Initiative Functional Diet Scale" in general (Steele et al., 2018). This speaks to the need for standardization of language and descriptors in providing best practices in therapeutic diet interventions.

TABLE 10 | An Example Description of Four Levels of Diets (current state)

Dysphagia Diet Fluids	
Thin Fluids	All fluids that are thin at room temperature: water/ice chips/juices/ tea/liquid nutritional supplements/ regular or strained soups/ice cream/jello.
Nectar Thick Fluids	Thin fluids that are thickened to the consistency of nectar and are sipped from a cup: nectar thick juices, milk, water, soup.
Honey Thick Fluids	Thin fluids that are thickened to the consistency of liquid honey but can be sipped from a cup: honey thick juices, milk, water, soup.
Pudding Thick Fluids	Thin Fluids that are thickened to the consistency of pudding and are eaten with a spoon: pudding thick juices/mild/water/soup/custards, high energy puddings/smooth yogurt.
Dysphagia Diet Textures	
Regular	All items are served unmodified.
Ready	Same as regular but roast meats are diced.
Diced Meat/Modified Vegetable	Most meats are diced/soft proteins are allowed whole (meatloaf); also allowed: bananas, watermelon, strawberries etc); not allowed: raw vegetables, brussel sprouts, large pieces of cauliflower, whole corn.
Minced meat/Modified Vegetable	Most meats are minced, soft protein items are allowed, nothing on a bun, no brussel sprouts, florets of cauliflower or broccoli, no stir fry (mince before serving); allowed: mashed potatoes, macaroni salads, bananas, sliced strawberries, and seedless watermelon.
Minced	Minced meats, vegetables, mashed potatoes, potato puffs, scalloped potatoes, cheese, peanut butter sandwiches, fresh bananas, minced strawberries, seedless watermelon.

Dysphagia Diet Fluids	
Pureed	All foods with a pudding type consistency, all entrees to be pureed, bread with diet syrup. No bananas, cottage cheese, oatmeal, old cereal, peanut butter.

The IDDSI Framework for Describing and Preparing Dysphagia Diet Levels



Speaking Valves (including the Passy-Muir Speaking Valve (PMV)

Speaking valves, including the Passy-Muir (positive closure) Speaking Valves (PMV) can improve voice quality and speech production while, at the same time, improving swallowing and reducing aspiration risks (Passy-Muir Incorporated, 2004). Aspiration is often problematic in individuals who have a tracheostomy, as these patients are essentially unable to achieve the apneic interval necessary for an efficient swallow or create the pressure necessary for optimal swallowing function. It is thought that normalization of subglottic air pressure, achieved through placement of a speaking valve, reduces the potential for aspiration and improves swallowing efficiency.

The valve may be attached to the 15mm connector found on most adult tracheostomy tubes (Dettelbach et al., 1995; Passy et al., 1993). With the speaking valve in place, a noticeable decrease in the amount aspirated has been observed. While wearing the valve, individuals also have the opportunity to more easily express themselves verbally (Bell, 1996). Passy et al. (1993) found that individuals began speaking almost immediately and their speech improved making it easier for them to communicate with hospital staff, doctors, and family. This ease of communication is very beneficial to the individual's ability to direct their own care related to feeding, swallowing, dysphagia diet, and diet preferences.

Within the literature, the benefits of the speaking valves have been supported. Manzano et al. (1993) found that individuals experienced a decrease in secretions and showed improvement in ability to cough with the PMV in place (Manzano et al., 1993). Further supporting its effectiveness, the volume of secretions appears to increase when the PMV is removed (Lichtman et al., 1995; Passy et al., 1993) .The use of a PMV has also been shown to significantly reduce aspiration (Elpern et al., 2000; Stachler et al., 1996) , provide the ability to safely ingest thin liquids (Suiter et al., 2003), improve oxygenation, decrease oral and nasal secretions, improve sense of smell, enhance airway clearance, and improve swallowing (Bell, 1996). To determine its effectiveness specifically within the ABI population more research is recommended.

Interventions for Dysphagia Management

The majority of studies addressing dysphagia have been conducted in individuals with stroke and there is limited research focusing specifically on dysphagia management in individuals with moderate and severe ABI. In individuals with stroke, interventions such as the McNeill Dysphagia Therapy Program have been used to facilitate swallowing function, indicating superior benefits such as dysphagia severity reductions and improve oral intake, when compared to traditional therapies (Carnaby-Mann & Crary, 2010; Carnaby et al., 2020). We found three studies that evaluated the effectiveness of interventions for dysphagia individuals with ABI.

TABLE 11 | Dysphagia Management Post ABI

Author Year Country Study Design Sample Size	Methods	Outcome
Yan et al. (2021) China RCT PEDro=5 N=60	**Population:** Severe TBI; *Test Group (n=30):* Mean Age=55.2±5.5yr; Gender: Male=18, Female=12; Mean GCS=11.83±2.64. *Control Group (n=30):* Mean Age=54.8±6.2yr; Gender: Male=21, Female=9; Mean GCS=11.46±3.13. **Intervention:** Patients in the control group received routine care while patients in the test group received evidence-based bundled care consisting of head nurses, primary nurses, speech therapists, physicians and dietitians. The bundle of care provided food intake	1. Both groups experienced an increase in MASA scores post intervention ($p<0.001$). 2. Compared with the control group, the MASA scores in the test group were significantly increased ($p<0.001$). 3. Compared with the control group, fewer participants had positive rates with the Evans Blue Dye test after intervention in the test group, and the difference was significant ($p<0.05$).

	training, diet and oral care, orofacial sensory training, neuromuscular electrical stimulation, and intermittent oro-esophageal tube feeding. **Outcome Measures:** Modified Mann's Assessment of Swallowing (MASA), Evans Blue Dye Test, Watian drinking water test, Functional oral intake scale (FOIS), Modified Beck Oral Assessment Scale (BOAS).	4. Watian drinking water test was significantly declined in the test group compared with the control group (P<0.05). 5. The FOIS scores of both groups significantly increased after intervention (P<0.001), and it was more significant in the test group (P<0.001). 6. Compared with the control group, BOAS scores in the test group were significantly decreased (P<0.05).
Jakobsen et al. (2019) Denmark RCT PEDro=8 N=10	**Population:** Severe ABI; TBI=1, Aneurism=2, Hypophysis Adenoma=1, Infarction=1, Intracerebral Hemorrhage=2, Meningioma=1, Subarachnoid hemorrhage=2; *Intervention Group (Intensified Nonverbal Facilitation of Swallowing* (n=5): Mean Age=53.8yr; Gender: Male=2, Female=2; Mean Time Post Injury=76.4±21.8d; Severity: Mean GCS=9.8±1.8. *Control Group Standard care* (n=5): Mean Age=45.6yr; Gender: Male=4, Female=1; Mean Time Post Injury=70.4±43d; Severity: Mean GCS=10.6±1.5. **Intervention**: All participants received 30 sessions of treatments (20 min, twice daily, for 3wk) in addition to daily rehabilitation program. Intervention group received an intensification of the nonverbal facilitation of swallowing through the Facial Oral Tract Therapy (FOTT) (20 min, twice daily, for 3wk), while the control group only received basic care of the face and mouth. Outcome measures were assessed at baseline and the end of the intervention. **Outcome Measures**: Functional Oral Intake Scale (FOIS), Penetration Aspiration Scale (PAS), Electrophysiological Swallowing Specific Parameters (EMBI), Maximum laryngeal elevation during swallows, Speed of laryngeal elevation, Frequency of swallowing and pumping jaw movement.	1. No significant group differences were observed at baseline. 2. The intensified intervention was feasible; however, the intervention with two extra treatments per day was considered very intensive for patients. 3. PAS and FOIS scores improved in both groups; however, there were no significant differences between groups for these outcomes (p>.05). 4. The mean maximum laryngeal elevation and median speed of laryngeal elevation increased in the intervention group and decreased in the control group. 5. Median swallowing frequency increased in both groups. 6. Except fatigue, no adverse event was reported as a direct result of intervention.
Nordio et al. (2019) Italy Case Series N=37	**Population:** Anoxic Brain Injury, N=37; Age Range=18-89yr; Gender: Male=28, Female=9; Mean Time Post Injury=Not Reported; Severity: GCS Range=3-8. **Intervention:** Retrospective review of individuals with ABI from San Camillo Hospital from 2011 to 2018 that received intensive rehabilitation program (1-2 hr/day, 5 days/wk) for communicative and swallowing disorders. Outcome measures were assessed within one week from hospital admission and after treatment. **Outcome Measures:** Incidence of Dysphagia, Aphasia, and Dysarthria, Functional Independence Measure (Muller-Lissner et al.), Therapy Outcome Measure (TOM), Functional Oral Intake Scale (FOIS).	1. Dysphagia was a frequent and severe outcome, while aphasia and dysarthria were less severe in participants. 2. FIM motor and cognitive scores improved significantly between initial assessment and assessment after treatment (p<0.05). 3. TOM score for dysarthria and FOIS score for dysphagia significantly improved after treatment (p<.05). 4. The presence of dysphagia decreased after treatment (35.15% patients preserved vs 67.57%) (p<0.05). 5. No significant improvements were observed for those with aphasia (p=0.18).

Discussion

In an RCT, Jakobsen et al. (2019) examined the effect of an intensification of the nonverbal facilitation of swallowing. While the intervention group received treatment using the Facial Oral Tract Therapy (FOTT) concept, the control group received stimulating activities in the facial oral tract, without facilitation of swallowing or verbal requests to swallow. The authors found that scores on the Penetration Aspiration Scale (PAS) and Functional Oral Intake Scale (FOIS) improved in both groups; however, no significant differences between groups were observed (Jakobsen et al., 2019).

In a PCT study, Yan et al. (2021) examined the effect of an evidence-based bundle of care model in individuals with dysphagia post severe TBI. While all participants received routine care, participants in the intervention group received bundled care by a group of healthcare professionals such as nurses, speech therapists and registered dietitians. Participants in the bundle of care group received oral training, including neuromuscular electrical stimulation, orofacial sensory training and orofacial exercise training. The authors found that, compared with the control group, the MASA scores, grading of Watian water drinking test, and FOIS scores were significantly improved in the intervention group; in addition, the positive rate with the Evans Blue Dye test was significantly reduced in patients with disorders of consciousness that received bundled care (Yan et al., 2021).

In a case series study, Nordio et al. (2019) investigated the impact of an intensive rehabilitation program for individuals with ABI with communicative and swallowing disorders. The dysphagia interventions were individualized for each participant based on their specific swallowing deficit and involved compensatory manoeuvre, postural adaptations during meals, food, and liquids modification, as well as effortful swallow exercises. The study revealed a significant improvement in Functional Oral Intake Scale (FOIS) score for dysphagia, presence of dysphagia, tracheal tube, and enteral nutrition from baseline to post-intervention (Nordio et al., 2019).

Conclusion

There is level 1b evidence (Jakobsen et al., 2019) that intensified facial-oral tract therapy in swallowing is feasible and may improve swallowing specific parameters in individuals with ABI.

There is level 2 evidence (Yan et al. 2021) that evidence-based bundle may improve swallowing function in individuals with severe TBI.

There is level 4 evidence (Nordio et al., 2019) that an intensive rehabilitation program for communicative and swallowing disorders may be effective in treating in individuals with anoxic brain injury.

KEY POINTS

- Intensified facial-oral tract therapy in swallowing may improve swallowing specific parameters in patients with ABI.
- Evidence-based bundled cared may be effective for improving swallowing function post TBI.
- An intensive rehabilitation program for communicative and swallowing disorders may be effective in treating dysphagia and dysarthria in patients with anoxic brain injury.

Oral Health Interventions

Oral hygiene and dental care have become an important component in treating patients post TBI (Clayton, 2012; Zasler et al., 1993). Management of proper oral hygiene decreases the medical risks associated with dysphagia and poor oral care. The actual provision of oral care is more challenging in patients with TBI given the frequent presentation of significant cognitive-communication issues including fatigue, reduced level of alertness, cooperation and comprehension, as well as a lack of physical recovery necessary to complete the task of brushing independently (Zasler et al., 1993). For the reasons listed, as well as improper or insufficient staff training, there may be less priority placed on providing mouth care as part of the overall care routine. It becomes important, to provide regular education about the beneficial effects of thorough oral hygiene practices from a social integration, comfort, medical, and safety management standpoint.

Oral biofilm (or plaque) is a combination of proteins/glycoproteins and bacteria. Following oral care, oral biofilm/plaque begins forming again in as little as 15 minutes. Within two hours, bacteria have multiplied, and this biofilm may even double in mass and begin forming complex networks of bacteria colonies that are able to communicate with each other. There is a four to six-fold increase in the incidence of aspiration pneumonia in people with periodontal disease and/or poor oral care (Maddi & Scannapieco, 2013). In individuals who are NPO (nothing by mouth) with enteral feeding for total nutrition there is no mechanical disruption of the biofilm through movement of food and liquid or by the tongue and oral muscles; therefore, biofilm accumulates more easily (including formation on the soft issues). For this reason, the role of thorough mouth care for individuals who are NPO becomes even more critical (written communication from Dr. Greenhorn-November 23, 2012).

Unlike oral care advice in the general population, mouth care in individuals with dysphagia is best performed before eating/drinking. The rationale is that the introduction of oral bacteria to the lungs via aspiration is more problematic than the food or liquid that is aspirated own their own. Brushing before eating/drinking for individuals with dysphagia means that bacteria do not have the opportunity to be introduced to the lungs even in “known aspirators”, thereby reducing the incidence of pneumonia

(Seguin et al., 2014). Many people with TBI may be more difficult to approach with regards to mouth care. For this reason, the key elements of care must be known so care is as efficient as possible. Clayton (2012) states "*education of staff regarding the importance of oral hygiene and obtaining quality oral care equipment is vital.*" Currently, there is very little evidence in the literature to suggest that oral care is routinely performed, particularly when the person with TBI is in hospital or long-term care (Kelly, 2010; Landesman et al., 2003; Talbot et al., 2005).

Education in oral health and good oral care is needed to reduce the risk of dysphagia and other associated complications that can result from a brain injury. Furthermore, research conducted in long-term care or acute care facilities reported a decline in mortality rates, risk for developing dysphagia, and risk of aspiration pneumonia with the introduction of an oral care program (Sarin et al., 2008; Watando et al., 2004).

TABLE 12 | Oral Health Post ABI

Author Year Country Study Design Sample Size	Methods	Outcome
Oral Hygiene		
Zasler et al. (1993) RCT USA PEDro=4 N=20	**Population:** TBI; Total Population Mean Age=30 yr; Gender: Male=14, Female=6; Time Post-Injury>1 mo; *Intervention Group* (n=10); Mean GCS=7; *Control Group* (n=10); Mean GCS=6. **Intervention:** Participants in the intervention group received verbal oral hygiene instructions and were supervised in the removal of plaque. Those in the control group did not receive any oral hygiene instructions. Assessments were done at baseline and follow-up (5-6 wk). **Outcome Measure**: Plaque index score.	1. No differences were found between the intervention and control group when examining the mean plaque scores at baseline (1.94 versus 2.12, p>0.05). 2. Following intervention, the mean plaque index scores for the intervention group was significantly lower than those of control group (1.06 versus 2.19, p<0.01).
Oral Hygiene for Dysphagia-Related Complications		
Seguin et al. (2014) France RCT PEDro=7 N=167	**Population:** Severe ABI, TBI=123, Cerebral Hemorrhage=44, Other=22; *Intervention Povidone-Iodine Group* (n=85); Mean Age=48yr; Gender: Male=60, Female=25; Mean Time Post Injury=6hr; Mean GCS=6. *Control Placebo Group* (n=82); Mean Age=48yr; Gender: Male=64, Female=18; Mean Time Post Injury=6hr; Mean GCS=6. **Intervention:** Participants were randomly assigned to either receive povidone-iodine for decontamination of the oropharyngeal tract, or placebo as the control group. **Outcome Measure:** Incidence of Ventilator-Associated Pneumonia (VAP), Mortality, Length of Stay in ICU (LOS-ICU), Length of Stay in Hospital (LOS).	1. VAP occurred in 31% of participants in the povidone-iodine group and 28% of participants in the placebo group, and the difference was not significant between groups (p=0.69).

Robertson & Carter (2013) Canada Case Control N=83	**Population:** TBI, Intracranial hemorrhage, tumor, Other. Standard oral care (Canadian Dental Association) Group (n=51): Mean Age=57yr; Gender: Male=27, Female=24. Enhanced oral care (EOC) group (n=32): Mean Age=61yr; Gender: Male=23, Female=9. **Intervention:** Participants in the SOC group received a standard protocol for oral hygiene and were reviewed retrospectively; participants in the EOC group were prospectively studied and received an enhanced oral hygiene protocol. The oral care kit was kept beside the person's bed and nurses were trained prior. The EOC consisted of brushing, mouth rinse, and swabs. **Outcome Measure:** Incidence of non-ventilator hospital-acquired pneumonia (NV-HAP).	1. A significant decrease in in the rate of NV-HAP was observed in the EOC group compared to the SOC group (p=0.039).

Discussion

In the Zasler study (1993), participants who were provided verbal oral hygiene instructions and taught to remove plaque had significantly less plaque on their teeth post intervention compared to the control group. Study authors suggest that this improvement can lead to greater integration back into society, as the potential negative consequences associated with poor oral hygiene have been addressed (Zasler et al., 1993). Verbal education appears to be sufficient to improve dental plaque control (Zasler et al., 1993). In a RCT conducted by Lam et al. (2013), multiple oral care protocols were examined including various combinations of instruction, mouth rinse and assisted tooth brushing. No significant differences were found between the three protocols when looking at the amount of oral opportunistic pathogens that developed.

Seguin et al. (2014), investigated the efficacy of povidone-iodine versus a placebo drug in reducing ventilator-associated pneumonia. The occurrence of ventilator-associated pneumonia, although reduced in the experimental group, was not significantly different from the control group (Seguin et al., 2014). Povidone-iodine was also shown to increase the risk of secondary infections including acute respiratory distress syndrome (Seguin et al., 2014). However, another study demonstrated reduced rates of non-ventilator hospital-acquired pneumonia among participants receiving enhanced oral care. Robertson and Carter (2013) found that individuals receiving the enhanced oral care protocol had a significant decrease in acquired pneumonia when compared to the standard oral care group (Robertson & Carter, 2013).

Conclusion

There is level 2 evidence (Zasler et al., 1993) that providing oral hygiene education to individuals post TBI results in a significant reduction of dental plaque, measured by the Plaque Index Score.

There is level 3 evidence (Robertson & Carter, 2013) that enhanced oral care may reduce rates of non-ventilator hospital-acquired pneumonia compared to standard oral care in mixed brain injury populations.

There is level 1b evidence (Seguin et al., 2014) that povidone-iodine is not more effective for reducing the incidence of ventilator-associated pneumonia compared to placebo in individuals post stroke or ABI.

KEY POINTS

- Oral hygiene education may result in a decrease in dental plaque.
- Enhanced oral care may reduce the rate of non-ventilator in hospital pneumonia in brain injured patients.
- Decontamination of oropharyngeal tract using povidone-iodine may not prevent ventilator-associated pneumonia in in ICU admitted brain injured patients.

Nutritional Interventions

Some nutrition topics and evidenced-based nutrition interventions are not discussed in this section that would commonly be used for ABI patients as the patient populations that this research evidence is based on is not specific to moderate to severe ABI patients. Therefore, these topics and evidenced-based nutrition interventions do not meet ERABI's methodology criteria. Some of these other nutrition topics include but are not limited to pressure injury nutrition assessment/treatment, further topics within enteral feeding initiation and management, malnutrition screening and management, progressing patients from enteral and/or parental nutrition to oral nutrition and oral nutritional strategies to maintain one's nutritional status. Please refer to non-ABI patient specific, evidenced based, nutrition resources such as ASPEN (American Society of Parental and Enteral Nutrition), PEN: Practice Based Evidenced in Nutrition, Dietitians of Canada and many other for further nutrition guidelines on these more generalized areas of nutrition practice.

Ensuring individuals with ABI have adequate nutrition is an important part of their medical management (Denes, 2004), as it has a critical impact on the person's recovery process and final outcome (Elovic, 2000). According to Denes (2004), individuals with severe ABI who present with severe malnutrition may have serious complications at the time of admission and during rehabilitation, including presence of contractures, heterotopic ossification and pressure sores, challenges in mobilization and a longer length of stay in rehabilitation units. Despite clinicians' efforts several factors make it difficult to avoid malnutrition in persons with ABI, beginning with the metabolic changes that occur post injury (Elovic, 2000). Post ABI, the damage to the metabolic control center causes more severe and protracted systematic responses than seen in many other forms of injuries. The former is a possible consequence of the change in feedback mechanisms post injury and the brain's critical role in triggering the metabolic

response (Young et al., 1992). Individuals with TBI often present with body composition changes such as weight loss, consumption of lean body mass, negative nitrogen balance, as well as water and salt retention (Kurtz & Rocha, 2020).

Secondary to ABI, a catabolic and counter regulatory hormone (glucagon and cortisol cortical) increase takes place (Loan, 1999). Deficiencies of follicle-stimulating hormones, luteinizing hormone, and growth hormone (GH) indicate alteration in the hypothalamic-pituitary feed-back mechanism that normally regulates metabolism (Loan, 1999). As a result of hypermetabolism and hypercatabolism, both energy and protein requirements will be elevated in the first several weeks following injury. Negative energy and nitrogen balance, which may exceed 30 grams per day, have been reported within the first week following injury (Bruder et al., 1994; Weekes & Elia, 1996; Wilson et al., 2001; Young et al., 1985). Unfortunately, although muscle wasting occurs as a consequence of bed rest and immobilization, only a portion of these losses are responsive to nutritional interventions (Behrman et al., 1995).

Incidence of Malnutrition

The incidence of malnutrition following ABI is difficult to estimate as there are no consistent criteria used, and relatively few studies have examined the issue. Given that ABI tends to occur in younger, previously healthy individuals, it is unlikely that pre-existing nutritional deficits are prevalent at the time of injury. Therefore, declines in nutritional parameters are most likely directly related to the metabolic effects of the injury. Brooke et al. (1989) reported an average weight loss of 13.2 kg from injury to rehabilitation admission, while Weekes and Elia (1996) reported 9.8 kg of weight loss from the time of injury to day 19 in four previously healthy young males. In the early rehabilitation phase, a substantial amount of participants are underweight (approximately 60%) (Brooke et al., 1989; Haynes, 1992); however, obesity has also been reported among individuals, typically in the chronic phase of recovery (Henson et al., 1993). Another factor which can contribute to malnutrition or dehydration following an ABI is diarrhea, which has been shown to occur in rates as high as 70% in those receiving enteral nutrition, and in relation to the use of antibiotics for over 1-week (Vieira et al., 2018). Vieira et al. (2018) reported that the individuals who had diarrhea, were also seen to have longer stays in the ICU and were attributed to enteral nutrition intolerance.

Hypermetabolism Post ABI

Hypermetabolism is a well-known metabolic sequela of ABI. Hypermetabolism has been defined as an increase in metabolic rate above that which is predicted using equations, which take into account age, sex, height, and weight (Souba & Wilmore, 1999). The hypermetabolic state, which is characterized by increased oxygen consumption and nitrogen excretion following injury, is thought to be mediated by an increase in: *i*) counterregulatory hormones such as epinephrine, norepinephrine and cortisol, *ii)* corticosteroids, and *iii)* proinflammatory mediators and cytokines (Kurtz & Rocha, 2020; Pepe & Barba, 1999) . Tremendous variability has been reported regarding the magnitude of the hypermetabolic state post ABI. The variations are likely due to the timing of the measurements, individual characteristics (i.e.,

initial level of injury, concomitant infections) and management (i.e., craniotomy, intubation, and sedation and/or barbiturate use, ambient temperature).

Resting Energy Expenditure (REE) represents the number of calories required for a 24-hour period by the body during a non-active period. Young et al. (1985) found REE to decrease consistently over time post ABI (151% to 116% over 22-day evaluation). Bruder et al. (1994) compared REE in persons with ABI who were weaned off from sedation, while others were re-sedated. REE increased to 143% of predicted values in those who were weaned from sedations, while the increases in REE were only 122% of predicted values in those who received additional sedation (Bruder et al., 1994), demonstrating that sedation can impact metabolic rates. Barbiturate use as it relates to REE was examined by Dempsey et al. (1985); the findings showed that mean REE was significantly lower during barbiturate therapy than without barbiturate therapy, when it was administered to those with failing intracranial pressure (ICP) ($p<0.01$) (Dempsey et al., 1985). Other factors that affected REE after head injury were evaluated by Robertson et al. (1984). The authors found that participants with GCS 4-5 had the highest REE at 168±53% of expected values, and was lowest in participants with GCS 6-7 at 129±31% of expected values (Robertson et al., 1984).

The evidence suggests that individuals with ABI are often hypermetabolic, with significantly higher resting energy expenditure in the acute period following the injury. Continued research in this area is needed help to establish meaningful guidelines regarding use of barbiturates and sedations as modifiable factors.

Fluid Consumption and the Frazier Free Water Protocol

To increase fluid consumption and decrease the risk of dehydration, the Frazier Free Water Protocol allows individuals who are receiving thickened liquids to be given regular, thin water in between meals in absence of food or other beverages. Thickened fluids do not quench thirst in the same way that regular thin water does. Therefore, the regular water, in combination with the recommended thickened fluids, works to assist some people in better meeting their daily hydration needs. Individuals who are NPO are can be permitted to have water following a successful swallowing screen; in addition, postural maneuvers when drinking water can also be used. The Frazier Free Water protocol states that, by policy, water is allowed for any individual NPO or on a dysphasic diet (Panther, 2005).

Enteral Nutrition

Enteral Nutrition (EN) consists of delivering complete nutritional requirements directly into the stomach, duodenum, or jejunum using a gastroenteric tube. EN is beneficial when individuals are unable to ingest nutrients independently, but their bodily functions still allow for the digestion of food. However, post-ABI, caloric and nutrient requirements may not always be met orally, and EN is used as supplementation. Individuals should be routinely monitored for signs of malnutrition and dehydration. In the early stages

of recovery, a significant percentage of individuals will be comatose and mechanically ventilated, precluding oral feeding. While enteral feeding is the preferred route of nutrient administration, feeding intolerance due to gastroparesis and ileus are common. Enteral feeding has been associated with a decrease in bacterial translocation and a reduced incidence of infection. Enteral feeding intolerance may be related to increased intracranial pressure (Ott et al., 1990). Medications may also play a role in delayed gastric emptying. Although the placement of feeding tubes into the small bowel may theoretically improve tolerance, placement can be difficult and empirical evidence of superiority is lacking. If intolerance is prolonged, parenteral feeding may be indicated (Cerra et al., 1997).

It should be noted that, even though several studies included in this module have used serum albumin and prealbumin as nutrition markers, their use as proxy measures of total body protein or total muscle mass is no longer recommended according to guidelines by the American Society for Parenteral and Enteral Nutrition Board of Directors (Evans et al., 2021).

TABLE 13 | Enteral Feeding for Nutritional Management Post ABI

Author Year Country Study Design Sample Size	Methods	Outcome
Carteron et al. (2021) France RCT PEDro=7 N=195	**Population:** ABI; TBI=95, Intracerebral Hemorrhage=24, SAH=50, Stroke=20, Other=6; *Enteral semi-elemental (SE) Group (n=100):* Median Age=57yr (range 44-65yr); Gender: Male=67, Female=33; Mean GCS=6 (range 3-7). *Enteral polymeric (P) Group (n=95):* Median Age=55 (range 40-65yr); Gender: Male=53, Female=42; Mean GCS=5 (range 3-7). **Intervention:** Patients were randomly assigned within 36hr of admission to the polymeric (P) or semi-elemental (SE) groups. The P group (n=95) received a hypocaloric (1.5 kcal/ml) polymeric formula (7.5 g/100ml of proteins, 5.8g/100ml of lipids, 17.0g/100ml of carbohydrates). The SE group (n=100) received a hypercaloric (1.5 kcal/ml) semi-elemental formula (9.4g/100ml of proteins, 6.5g/100ml of lipids, 13.5g/100ml of carbohydrates). **Outcome Measures:** Mortality, Aspartate aminotransferase (AST) levels, Alanine aminotransferase (ALT) levels, Gamma-glutamyl transferase (GGT), Protein intake, Albumin levels, Length of Mechanical Ventilation, Incidence of Pneumonia, Length of ICU Stay (LOS-ICU).	1. Daily protein intake was significantly higher in the SE group compared to the P group ($p<0.0001$). 2. The primary endpoint did not differ significantly between groups ($p=0.73$). 3. There were no significant differences in albumin ($p<0.4130$) and prealbumin ($p<0.4353$) levels between groups.

Author Year Country Study Design Sample Size	Methods	Outcome
Zhang et al. (2020) China RCT PEDro= 6 N=82	**Population:** Severe TBI; *Observation group (n=41):* Mean Age=64.7±6.6yr; Gender: Male=24, Female=17; Mean GCS=5.67±2.21. *Control group (n=41):* Mean Age=64.3±5.4yr; Gender: Male=26, Female=15; Mean GCS=5.42±2.39. **Intervention:** Control group was given enteral nutrition (EN) on basis of routine treatment. Observation group was given EN combined with parenteral nutrition (PN) nursing intervention. **Outcome Measures:** Hemoglobin, Total protein (TP), Albumin (Alb), Prealbumin (Prealb), Glasgow Outcome Scale (GOS).	1. Hb, TP, Alb and Prealb levels in the observation group were significantly higher than in control ($p<0.01$) after treatment. 2. Average GOS after treatment was higher in the observation group (3.42±1.71) than in the control (2.43±1.52) ($p<0.05$). 3. The incidence of adverse reactions such as vomiting, diarrhea, abdominal distension, constipation, gastrointestinal bleeding, and lung infection in the observation group was lower than that in the control group ($p<0.05$).
Justo Meirelles & de-Aguilar-Nascimento (2011) Brazil RCT PEDro=5 N=22	**Population:** TBI; *Enteral Nutrition (EN) Group*: Mean Age=31yr; Gender: Male=11, Female=1; Mean GCS Score=9. *Total Parenteral Nutrition (TPN) Group*: Mean Age=31yr; Gender: Male=9, Female=1; Mean GCS Score=9. **Intervention:** Participants were randomized to receive either EN or TPN. Both groups received a 25-30 kcal/kg/day and 1.5 g/kg/day of protein. EN was administered via 8 or 10F oro- or naso-enteral feeding tube in gastric position with pump infusion. TPN was administered via central venous access. Participants assessed daily for 5 days. **Outcome Measures:** Mortality, morbidity, ICU Length of Stay (LOS), days of mechanical ventilation, amount of calories and protein received/d, blood glucose, albumin, urea, creatinine, C-Reactive Protein (CRP), urinary urea (N).	1. No significant differences were found in morbidity and mean ICU LOS between the EN and TPN groups. 2. The mean serum glucose level in TPN group was significantly higher than EN group ($p<0.001$) 3. A progressive caloric deficit occurred in both groups ($p=0.001$) without any between group difference, despite the everyday increase in the number of calories. 4. Nitrogen was delivered more efficiently in TPN group than EN group, and TPN group received higher amounts of nitrogen than the NE group ($p < 0.05$). 5. There was a trend ($p = 0.06$) of 24 h urinary N loss to be greater in TPN group; however, both groups showed similar significant improvements ($p=0.001$) in the nitrogen balance as a result of nutritional therapy.
Nataloni et al. (1999) Italy RCT PEDro=4 N=45	**Population:** TBI; Gender: Male=31, Female=14. *Group A (n=15)*: Mean Age=45.6yr, Mean GCS Score=6. *Group B (n=15)*: Mean Age=46.3yr, Mean GCS Score=6. *Group C (n=15)*: Mean Age=44.2yr, Mean GCS Score=5. **Intervention:** Participants were randomly administered one of the following feeding conditions: enteral (Group A), parenteral (Group B), or both enteral and parenteral (Group C). Those who participated were expected to stay in ICU for ≥3 days. Feeding began within 2 days of ICU admission and continued for the length of stay. Assessments were made at baseline and after (day 3, 7 and 11). **Outcome Measures:** Serum pre-albumin, Retinol-Binding Protein (RBP), nitrogen balance.	1. Nitrogen balance, which was negative for all groups, improved over the course of treatment; however, it only significantly improved in Group A by day 11 ($p<0.0001$). 2. Pre-albumin and RBP significantly increased in all groups, and the increase was significantly greater in Group A compared to both Group B ($p<0.001$) and Group C ($p<0.01$). 3. Significant differences in the level of pre-albumin began at day 3 ($p<0.01$) while the differences in the level of RBP began at day 7 ($p<0.01$).

Author Year Country Study Design Sample Size	Methods	Outcome
Borzotta et al. (1994) USA RCT PEDro=4 N=49	**Population:** TBI; Gender: Male=40, Female=9; *Early Parenteral Nutrition (TPN) Group (n=21):* Mean Age=28.9yr; Mean GCS Score=5.4. *Enteral Feeding (ENT) Group (n=27):* Mean Age=26.2yr; Mean GCS Score=5.2. **Intervention:** Participants were randomized to either TPN group or ENT. TPN tapering was began at day 5 for converting to gastric feeding. The ENT group had enteral feeding through jejunal tubes. Assessments made daily for 10 days and weekly for 5wk thereafter. **Outcome Measures:** Measured Energy Expenditure (MEE), Nitrogen Balance, Serum Transferrin levels, Serum Bilirubin, Serum Albumin, Serum Gamma Glutamyl-Transferase, Incidence of Infection.	1. No significant differences noted for nitrogen excretion or balance, energy expenditures, meeting nutritional goals, and frequency of infections. 2. Complications such as hyperglycemia ($p<0.05$) and diarrhea ($p<0.05$) were more common among participants receiving TPN. 3. Efficiency of feeding, measured by ratio of calories to MREE, showed an advantage for TPN at day 3, but none after. 4. There were no differences in mortality at the end of follow-up.
Young et al. (1987) USA RCT PEDro=5 N=96	**Population:** Severe Head Injury. *Total Parenteral nutrition (TPN) Group*: Mean Age=29.9 yr, Gender=Not Reported, GCS Score=6.7±0.34. *Enteral feeding (EN) Group*: Mean Age=33.8 yr, Gender=Not Reported, GCS Score=6.8±0.62. **Intervention:** Participants were randomly assigned to receive either TPN or EN. TPN was initiated within 48 hr post-injury. EN was initiated when tolerated by patients. Study went from admission to day 18. Assessments made every 6 hr in the ICU, or 1x/day in the hospital ward. **Outcome Measures:** Intracranial pressure (ICP), serum glucose levels.	1. No significant differences were found between groups in peak daily ICP; ICP was >20 mmHG in 75% of the TPN participants and 73% of the EN participants. 2. Standard therapy was ineffective in controlling elevated ICP in 36% of the TPN and in 38% of the EN group. 3. There were no significant between-group differences in serum osmolality. 4. For the first 12 days, the TPN group received more calories and protein than the EN group ($p=0.0001$). 5. There was a significant day × nutrition group interaction ($p<0.0001$); serum glucose levels were higher in the TPN group for the first 13 days post injury than EN group who had increased mean serum glucose content after 13d.
Hadley et al. (1986) USA RCT PEDro=4 N=45	**Population:** TBI; N=35; Total Population Median Age=28yr. *TPN group (n=24)*: Mean Age=Not reported, Gender: Male=22, Female=2, Mean Admission GCS=5.8. *EN group (n=21)*: Mean Age=Not reported, Gender: Male=18, Female=3; Mean Admission GCS=5.9. **Intervention:** Participants were randomly assigned to receive either total parenteral nutrition (TPN) or enteral nutrition (EN). Participants received high nitrogen and calorie feedings for a 14-day period of the study to try to obtain a positive nitrogen and calorie balance. Nitrogen loss was measured every other day. **Outcome Measure:** Urinary nitrogen levels.	1. Participants who received TPN achieved significantly higher mean daily nitrogen intakes ($p<0.01$) and losses ($p<0.001$) compared to those who received EN. 2. There was no significant between-group difference in nitrogen balance.

Author Year Country Study Design Sample Size	Methods	Outcome
Rapp et al. (1983) USA RCT PEDro=4 N=38	**Population:** TBI; *Standard Enteral Nutrition (SEN) Group (n=18)*: Mean Age=34.9yr; Gender=Not Reported, Mean GCS Score=7.2. *Total Parenteral Nutrition (TPN) Group (n=20)*: Mean Age=29.2yr; Gender=Not reported, Mean GCS Score=7.7. **Intervention:** Participants were randomly assigned to either the SEN or TPN group. TPN therapy was initiated within 48 hr of admission. EN was given via nasogastric tubes and initiated when tolerated. **Outcome Measures:** Glasgow Coma Scale (GCS), Mortality, Serum Transferrin Levels, Albumin Levels, Calorie Intake, Nitrogen balance, Serum glucose levels,	1. No baseline between-group differences except for mean peak temperature during the first 24 hr of hospitalization; TPN group had a higher mean temperature than SEN group (38.6ºC versus 38.0ºC; p=0.02). 2. Within the 18-day period, 8 of the 18 participants died in the SEN group compared to 0 deaths in the TPN group (p<0.0001). 3. The TPN group had a significantly greater mean intake in nitrogen/d then the SEN group (10.2 gm versus 4.0 gm; p=0.002); the overall nitrogen balance was also significantly different between groups (p=0.002). 4. No significant between group difference was found in serum albumin levels over time.
Kofler et al. (2018) Austria Case Series N=17	**Population:** Poor-grade subarachnoid hemorrhage (SAH) (n=17); Median Age=57yr (range 48-69); Gender: Male=7, Female=10. **Intervention:** Patients received early enteral nutrition (EN) within 24 hr after aneurysm repair via nasogastric tube. After 24 hr, standard EN (1 kcal/ml) was initiated with a flow rate of 20–25 ml/h and gradually increased to target 20–25 kcal/kg/ d. Flowrate was adapted to gastrointestinal tolerance and not increased if gastric residual volume (measured every 6 h) exceeded 250 ml. If 80% of calculated calories was not achieved by day 4, supplemental parenteral nutrition (PN) was given. Patients were monitored using cerebral microdialysis (CMD). **Outcome Measures:** Serum glucose, CMD-glucose, CMD-lactate, CMD-pyruvate, CMD-LPR, CMD-glutamate	1. Serum glucose levels significantly increased after 3–6 hr (p<0.001) compared to baseline (138.9±3.9 mg/dl), with the maximum increase at 4 hr (167±8.6 mg/dl). 2. The mean baseline CMD-glucose concentration was 1.59±0.13 mmol/l, which increased during the intervention to a maximum of 2.03±0.2 mmol/l after 5 hr (p<0.001). 3. Serum glucose concentrations were significantly associated with CMD-glucose levels (p<0.001) and higher overall CMD glucose levels in normal appearing brain tissue (p<0.001). 4. There was no change over time in CMD-lactate, CMD-pyruvate, CMD-LPR, or CMD-glutamate.
Chapple et al. (2016) Australia Case Series N=37	**Population:** Moderate-severe TBI=37; Mean Age=45.3yr; Gender: Male=32, Female=5; GCS Range=3-12. **Intervention:** Data from ICU admitted individuals with TBI, including the nutrition methods data, were gathered and analyzed to quantify energy and protein delivery and deficits over entire hospitalization period. Protein intake and energy levels quantified during individuals' stay in the Intensive Care unit (ICU; 530 days) and once moved to ward-based care (982 days) for a total of 1512 days. Protein and nutrients	1. Enteral feeding (EN) was administered to 34 participants while in ICU and 18 in the ward. 2. 32 participants completed oral feeding at least once (mean=17.5 days), with 20 beginning in ICU and 12 in the ward. 3. There was less absolute energy (p=0.015) and protein (p=0.001) intake in ICU than the ward according to FW8. 4. Participants met their absolute requirements for energy and protein 83% and 75% of the time, respectively.

Author Year Country Study Design Sample Size	Methods	Outcome
	consumed calculated by comparison of weight before and after each meal for 3 days/wk. **Outcome Measures:** Dietitian clinical assessments via Food Works 8 (FW8) dietary analysis software.	5. Larger difference in prescribed vs actual energy intake in the ward than ICU (p=0.039), with no significance for protein intake (p=0.278). 6. More contribution from EN than oral for both energy (p=0.488) and protein (p=0.373), and those that exclusively were EN had smaller energy deficits than oral feeding (p=.016).
Fan et al. (2016) China PCT N=40	**Population:** Severe TBI, N=120, Total Population Mean Age=41.69yr; Gender: Male=62, Female=58. GCS Range=6-8 **Intervention:** Participants were assigned to receive nutrition Enterally (EN) (n=40), Parenterally (PN) (n=40), or combined (EN+PN) (n=40), supported by nutritional therapies. Measures were taken at day 1 and day 20. **Outcome Measures:** Levels of lymphocytes and Immunoglobulins, Serum Total Protein, Albumin, Pre-albumin, Hemoglobin, Complication Occurrence Rate, Length of Stay (LOS), Mortality rate.	1. Total serum protein was significantly decreased in the PN group (p<0.01) compared to serum protein on day 1, whereas total serum protein was significantly increased in EN and EN+PN groups (p<0.01). 2. The EN group had significantly higher rates of diarrhea (p<0.01) compared to the PN and EN+PN group. 3. Stress ulcers were significantly higher in the PN group (p<0.01) than the other two groups. 4. The EN group had significantly higher rates of aspirated pneumonia (p<0.01). The EN group had the lowest rates of pyemia (p<0.01). 5. The EN+PN group had the lowest rates of hypoproteinemia (p<0.01) and intracranial infection (p<0.01).
Horn et al. (2015) USA PCT N=1701	**Population:** TBI, N=1701; *Enteral Nutrition (EN) Group (n=451)*: Mean Age=38.5yr; Gender: Male=326, Female=125; Mean Time Post Injury=31.9 days; *No EN Group (n=1250)*: Mean Age=47.1yr; Gender: Male=895, Female=355; Mean Time Post Injury=19.8 days. **Intervention:** Participants admitted to an inpatient rehabilitation center post TBI were grouped into either EN (>1 days on EN) or no EN (<1 day or no days). Analysis of demographic and treatment data to determine the relationship between EN and participants outcomes. **Outcome Measures:** Functional Independence Measure, Comprehensive Severity Index (CSI), chart reviews, weight loss, Length of Stay (LOS).	1. Upon admission, high brain injury score on CSI, low FIM motor score, and having moderate-severe dysphagia were the strongest predictors of needing EN (p<0.001; c statistic=0.903). 2. Participants that received EN at standard or high protein concentrations for >25% of their stay (mean=19 days) had significantly better FIM discharge scores (p<0.030). 3. EN with a high protein formula for >25% of hospital stay was significantly associated with an almost two-pound weight gain from admission to discharge, while participants that did not receive EN lost two pounds (p=0.001).
Clifton et al. (1984) USA	**Population:** Severe Head Injury; N=14, Mean Age=27.8yr; Gender: Male=12, Female=2; GCS Score Range=3-8; Mean Time Post Injury=2 hr.	1. Mean values of REE ranged from 2135±374 Kcal on 1-3 days to 2504±582 Kcal on 7-9 days, which was not statistically significant.

Author Year Country Study Design Sample Size	Methods	Outcome
Case Series N=14	**Intervention:** The caloric expenditure and nitrogen balance of enteral nutrition fed individuals was measured by indirect calorimetry, acutely over the first 9 days of onset, and up to 28 days post injury. **Outcome Measures:** Resting Energy Expenditure (REE).	2. The mean REE ranged from 102%-170% of predicted values, over the 9 days of study. 3. A single participant who received barbiturates had a REE lower than predicted (79%). 4. Among participants who were non-sedated and non-paralyzed, REE was 138% of predicted values. 5. There were no significant changes in REE over the 9 days and no associations were noted between GCS and REE.

Discussion

In an RCT, Carteron et al. (2021) found that both hypocaloric polymeric EN regimen and Hypercaloric semi-elemental EN regimen had the same effect of nutritional outcomes including albumin and pre-albumin levels, except for the daily protein intake level which was higher in hypercaloric semi-elemental EN regimen post TBI.

In another RCT, Zhang et al. (2020) reported that EN combined with PN for individuals with TBI showed greater improvement in the levels of hemoglobin, albumin, pre-albumin, total protein, and the outcomes, and lower rates of adverse effects and complications, when compared to just EN administration.

In a case series, Chapple et al. (2016) investigated EN versus oral feeding. The results demonstrated a significantly greater energy deficit for participants receiving nutrition orally versus EN; however, protein deficits were similar. In addition, it was found that ward admission resulted in significantly higher levels of caloric intake prescribed than intensive care unit (ICU) admission (Chapple et al., 2016).

Fan et al. (2016) conducted a prospective controlled trial comparing EN versus PN versus combined EN and PN. Total serum protein, pre albumin, and hemoglobin were significantly decreased in the PN group, which corresponds to a degradation in nutritional status. While, in the EN and EN+PN groups, total serum and protein levels significantly increased after nutritional treatment. Therefore, the authors suggest a combination of EN+PN to improve prognosis and nutritional status for participants post injury (Fan et al., 2016b).

To date only two studies have looked at the general effectiveness of EN in an ABI population (Clifton et al., 1984; Horn et al., 2015). It was found that EN, when compared to no EN, resulted in trends towards smaller weight changes, improved FIM scores (motor and cognitive function), and longer length of stay, although, these between-group differences did not reach statistical significance (Horn et al., 2015). Clifton et al. (1984) examined the REE of those being treated with EN and found that REE was higher

than predicted, specifically with those participants who were not sedated. Further research is needed to better understand any potential benefits of EN outside of direct caloric or weight measures.

With respect to nitrogen balance, Justo Meirelles and de Aguilar-Nascimento (2011) also evaluated the effects of EN and PN in 22 participants with moderately severe TBI and found that parenteral nutrition delivered nitrogen more effectively. Both groups received increasing quantities of nitrogen each day, with those in the total parenteral nutrition (TPN) group receiving significantly more. Despite the increased daily loss of nitrogen, all participants showed significant improvement in nitrogen balance as a result of nutritional therapy (Justo Meirelles & de Aguilar-Nascimento, 2011). Nataloni et al. (1999) studied the effects of EN, PN, or both in a group of participants with ABI in the intensive care unit. Even though there was a negative nitrogen balance in all groups, all showed improvement over the course of the study. However, a positive nitrogen balance was only seen in the enteral group. Furthermore, other studies have found no difference in nitrogen balance between PN and EN (Borzotta et al., 1994; Hadley et al., 1986; Hausmann et al., 1985).

Young et al. (1987) investigated the effects of TPN versus EN administration on ICP levels in 95 severely brain-inured participants. Participants were randomly assigned to receive TPN or EN and ICP pressure was monitored, as well as serum glucose levels and hyperosmolality. No significant differences were observed between groups in relation to ICP levels or hyperosmolality, suggesting that EN and TPN can be administered safely to severely brain injured individuals without causing serum hyperosmolality or affecting ICP therapy.

It should be noted that, in clinical practice, optimal feeding methods should be decided by the clinician based on the patient individual needs and nutrition requirements.

Conclusions

There is level 1b evidence (Carteron et al., 2021) that both hypocaloric polymeric EN regimen and Hypercaloric semi-elemental EN regimen had the same effect of nutritional outcomes including albumin and pre-albumin levels, except for the daily protein intake level which was higher in hypercaloric semi-elemental EN regimen post TBI.

There is level 1b evidence (Zhang et al., 2020) that EN combined with PN for individuals with TBI showed greater improvement in the levels of hemoglobin, albumin, pre-albumin, total protein, and the outcomes, and lower rates of adverse effects and complications, when compared to just EN administration.

There is level 2 evidence (Justo Meirelles & de-Aguilar-Nascimento, 2011) that TPN delivered nitrogen more efficiently than EN therapy in individuals post TBI. However, both groups showed a significant improvement in nitrogen balance as a result of nutritional therapy.

There is level 2 evidence (Nataloni et al., 1999) that enteral feeding may be effective for improving nitrogen balance, while also increasing serum pre-albumin and RBP levels compared to parenteral nutrition and enteral plus parenteral nutrition in individuals post head injury.

There is level 2 evidence (Borzotta et al., 1994) that individuals post closed head injury treated with TPN or EN had no differences in nitrogen balance, energy expenditures, meeting nutritional goals and frequency of infections. However, enteral feeding post ABI may lead to decreased rates of hyperglycemia and diarrhea compared to parenteral nutrition.

There is level 2 evidence (Young et al., 1987) that intracranial pressure and serum osmolality are not affected by TPN or EN interventions in individuals post severe head injury.

There is level 2 evidence (Hadley et al., 1986) that individuals post TBI treated with NG or PTN had no significant changes in nitrogen balance, although, NG may be more effective in reducing nitrogen intake and nitrogen loss, when compared to PTN.

There is level 2 evidence (Rapp et al., 1983) that enteral feeding may reduce mean intake of nitrogen compared to parenteral nutrition in individuals post head injury

There is level 2 evidence (Fan et al., 2016) that enteral feeding may increase serum protein, the rate of aspirated pneumonia and diarrhea when compared to parenteral nutrition or combined enteral-parenteral nutrition post ABI.

There is level 2 evidence (Horn et al., 2015) that standard enteral nutrition or high protein formulas (greater than 20% of calories from protein) resulted in better FIM motor and FIM cognitive scores at discharge and less weight loss than similar patients not receiving enteral nutrition post TBI.

There is level 4 evidence (Kofler et al., 2018) that EN improved interstitial brain glucose levels in individuals with poor-grade sub-arachnoid hemorrhage, and this method of nutrition administration can be implied in the glucose management in these patients.

There is level 4 evidence (Chapple et al., 2016) that enteral feeding may be effective for meeting energy and protein requirements, while also contributing to a smaller protein deficit, compared to oral feeding in individuals post TBI.

There is level 4 evidence (Clifton et al., 1984) that individuals post head injury may expend more energy when on enteral nutrition than predicted by equations, and that this effect may be greater for non-sedated individuals.

KEY POINTS

- There is conflicting evidence regarding which method of feeding (EN or PN) is optimal to deliver nitrogen, meet required energy expenditures, nutritional goals and prevent complications.
- Enteral nutrition with high protein formulas may improve FIM motor and cognitive scores and result in less weight loss.
- For those with ABI being provided with enteral nutrition, energy expenditure levels may be beyond those predicted by equations.
- Enteral feeding may help to improve required interstitial brain glucose for people with severe brain injuries.

Timing

Early enteral feeding (EEF) is desirable to prevent intestinal mucosal atrophy and to preserve gut integrity (Kurtz & Rocha, 2020); although, as previously noted, feeding intolerance occurs frequently.

TABLE 14 | Timing of Enteral Feeding for Nutritional Management Post-ABI

Author Year Country Study Design Sample Size	Methods	Outcome
Chourdakis et al. (2012) Greece RCT PEDro=6 N=59	**Population:** TBI; *Delayed Enteral Feeding (DEF) Group (n=25)*: Mean Age=33.3yr; Gender: Male=21, Female=4; Mean GCS Score=5.22. *Early Enteral Feeding (EEF) Group (n=34):* Mean Age=36.13yr; Gender: Male=26, Female=8; Mean GCS Score=5.81. **Intervention:** Participants admitted to the ICU were randomly allocated to receive either DEF (2-5 days post admission) or EEF (initiated within the first 24-48 hr of admission). Measurements were taken on day 1, 6 and 12. **Outcome Measures:** Mortality, Length of ICU Stay (LOS-ICU), Resting energy expenditure (REE), Thyroid-stimulating hormone (TSH), Free Triiodothyronine (FT3), Free Thyroxine (FT4).	1. The EEF group began enteral feeding approximately 31hr post admission and the DEF group began approximately 77hr post admission. 2. Kilocalories administration was lower in the DEF group compared to the EEF group ($p<0.01$). 3. Several endocrine changes were noted for the groups, with the EEF group showing significant improvements compared to the DEF group ($p<0.05$). No differences were noted in mortality and morbidity in either group despite enteral feeding.

Author Year Country Study Design Sample Size	Methods	Outcome
Minard et al. (2000) USA RCT PEDro=5 N=27	**Population:** TBI; *Early Group (n=12)*: Mean Age=30yr; Gender: Male=9, Female=3; Mean GCS Score=7, Time Post-Injury=≤6 hr. *Late Group (n=15)*: Mean Age=36yr; Gender: Male=10, Female=5; Mean GCS=7, Time Post-Injury=≤6 hr. **Intervention:** Participants were randomly assigned to either early (within 60 hr of injury) or late enteral feeding. The late group received feeding when tolerated by the participant (i.e., gastroparesis was resolved). **Outcome Measures:** Calorie Intake, Mortality, Length of Hospital Stay (LOS), Length of ICU Stay (LOS-ICU), Duration of ventilation, Incidence of Infection, Incidence of Pneumonia.	1. No significant differences between groups regarding mortality, length of stay, ventilator days, number of infections per individual or participants with pneumonia. 2. Admission GCS score was a good predictor of infection ($p<0.003$), Length of stay in the ICU ($p<0.02$), and ventilator days ($p<0.007$).
Taylor & Fettes (1998) UK RCT PEDro=4 N=82	**Population:** Head Injury. *Intervention Group (n=41)*: Median Age=34yr, Gender=Not specified, Median Best Pre-ventilation GCS=9. *Control Group (n=41)*: Median Age=28yr, Gender=Not specified, Median Best Pre-ventilation GCS=8. **Intervention:** Participants were randomly assigned to receive either the standard Enteral Nutrition (EN) or the early EN. EN was initiated from day 1; however, in the control group, EN was gradually increased from 15 mL/hr up to estimated energy and nitrogen requirements. In the intervention group, feeding was administered at a rate that met estimated energy and nitrogen requirements. **Outcome Measures:** Nutritional intake, nitrogen balance, volume of gastric residuals, incidence of pneumonia.	1. Overall, participants received EN during 57% of the potential feeding time, with the longest interruption to feeding time coming from the rest period (13%). 2. Participants receiving early EN had a greater energy and nitrogen intake compared to standard EN patients over the initial week following brain injury ($p<0.02$). 3. Intervention participants received a higher volume of enteral fluid ($p<0.02$) but did not have a higher incidence of pneumonia or aspiration.
Ohbe et al. (2020) Japan Cohort N=3080	**Population:** TBI=3080; *Intervention Group (Early Enteral Nutrition) (n=1100)*: Mean Age=75yr; Gender: Male=725, Female=375; Mean Time Post Injury=Not Reported; Severity: GCS=<8.; *Control Group (Delayed Enteral Nutrition) (n=1980):* Mean Age=74yr; Gender: Male=1276, Female=704; Mean Time Post Injury=Not Reported; Severity: GCS=<8. **Intervention:** Analysis of the Japanese Diagnosis Procedure combination inpatient database of individuals with TBI from 2014 to 2017 that received early (within 2d of admission) or delayed enteral nutrition (3-5d after admission). **Outcome Measures**: Mortality, Nosocomial Pneumonia	1. No significant differences in in-hospital mortality were observed between groups (0.3%; 95% CI: -3.7%, 3.1%). 2. The proportion of participants with nosocomial pneumonia was significantly lower in the group that received early enteral nutrition than the delayed group (-3.2%; 95% CI: -5.9%, -.4%).
Azim et al. (2016)	**Population:** Severe TBI, *Early Tube Feeding (TF) group (n=58)*: Mean Age=39.4yr; Gender: Male=46,	1. There were no significant differences between groups in terms of mortality as a

Author Year Country Study Design Sample Size	Methods	Outcome
United States Cohort N= 90	Female=12; Median GCS=3. *Late TF group (n=32)*: Mean Age=45.7yr, Gender: Male=20, Female=12, Median GCS=3. **Intervention:** Data from individuals who received tube feeds during the ICU admission during a 3-year period were analyzed. Outcome of participants who received early tube feeding (<24 hr) were compared to those who had late tube feeding (>24 hr). **Outcome Measures:** Mortality, pneumonia, aspiration, bacteremia, ICU-free days, ventilator-free days.	result of early versus late tube feeding (p=0.44). 2. There were no significant differences in general complications (p=0.38), Hospital LOS (p=0.24) ventilator days (p=0.24), and discharge GCS (p=0.66) measures between groups. 3. The pneumonia rate (p=0.04) and ICU LOS (p=0.03) were significantly higher in the early TF group.
Dhandapani et al. (2012) India Cohort N=67	**Population:** Severe TBI; Time Post-Injury ≤24 hr; Total Population GCS≤8. Early *enteral feeding (EN) (≤3 days) group*: Mean Age=31.7 yr, Gender=Not reported. *Median EN (4-7 days) Group*: Mean Age=34.4 yr, Gender=Not Reported. *Late EN (>7 days) group*: Mean Age=37.2 yr, Gender=Not reported. **Intervention:** Participants were divided based on the day attained total enteral feeding, and the outcomes were compared between the groups. The volume of feed was increased gradually in keeping with an individual's gastric tolerance. **Outcome Measures:** Glasgow Outcome Scale (GOS), Mid-Arm Circumference (MAC), Mid-Arm Muscle Circumference (MAMC), and serum total protein.	1. Late EN group lost significantly more MAC and MAMC compared with early EN (p≤0.001). 2. Analysis of total serum protein revealed that more malnutrition was seen in the late EN group(p≤0.005). 3. At the 3 and 6 months follow-up, those receiving total enteral feeding within the first 7 days were more likely to have favorable outcomes on the GOS.

Discussion

Chourdakis et al. (2012) compared delayed enteral feeding with EEF in 59 individuals post severe TBI. Although rates of complications were comparable between groups, the length of feeding for the EEF group was significantly shorter than the length of feeding for the delayed group. Hormonal measurements also indicated that those in the early group showed significant improvements on several hormonal measures (Chourdakis et al., 2012).

Minard et al. (2000) and Azim et al. (2016) found that timing of enteral feeding had no significant impact on mortality, number of infections, ventilator days, or incidence of pneumonia (Azim et al., 2016; Minard et al., 2000). Ohbe et al. (2020) also observed no significant differences in in-hospital mortality between participants who received early versus late EN. However, contrary to the findings of the two studies discussed above, the early EN group in Ohbe et al. (2020) study had significantly lower incidence of pneumonia post-intervention compared to the late EN group (Ohbe et al., 2020).

In a prospective study comparing total EN at various time points (within 3 days, 4-7 days, and after 7 days) there were unfavourable outcomes associated with total EN after 3 days (Dhandapani et al., 2012).

Those who began later lost significantly more mid-arm circumference and mid arm muscle circumference and had worse malnutrition. At the third and sixth month follow-ups, those receiving total EN within the first 7 days were more likely to have favourable outcomes on the GOS (Dhandapani et al., 2012).

A Cochrane review by Yanagawa et al. (2000) identified six RCTs that addressed the timing to initiation of feeding and mortality as an outcome. The relative risk for death associated with early nutritional support was 0.71 (95% CI 0.43-1.16). The pooled relative risk from three trials, which also assessed death and disability, for early feeding was 0.75 (0.50-1.11). Although the results were not statistically significant, it was concluded that early feeding may be associated with a trend towards better outcomes in terms of survival and disability (Yanagawa et al., 2000).

Conclusions

There is level 1b evidence (Chourdakis et al., 2012) that early enteral nutrition may improve the hormonal profile of individuals post TBI compared to delayed enteral feeding.

*There is level 2 evidence (Minard et al., 2000**)** that early versus late enteral feeding has a similar effect on mortality, number of infections, ventilator days, or incidence of pneumonia in individuals post TBI.*

There is level 2 evidence (Taylor & Fettes, 1998) that early enteral nutrition may improve energy and nitrogen intake compared to standard enteral nutrition in individuals post head injury.

There is level 2 evidence (Ohbe et al., 2020) that early enteral nutrition may result in lower incidence of nosocomial pneumonia than late enteral nutrition.

There is level 2 evidence (Azim et al., 2016) that early and late enteral feeding did not have different impacts on mortality, general complications, ventilator days, hospital length of stay, and GCS at discharge. However, it was shown that early enteral feeding may result in longer length of stay in ICU, and higher rates of pneumonia.

There is level 2 evidence (Dhandapani et al., 2012) that late total enteral feeding can result in reduced arm circumference, worse malnutrition, and more disability compared to early total enteral feeding in individuals post TBI.

KEY POINTS

- Early enteral nutrition may be more beneficial than standard or late enteral nutrition for several patient outcomes post ABI, including survival and disability outcomes.

Administration Strategies

Decision making for nutritional support after brain trauma may be different for every patient. Jacobs et al. (2004) presented factors that should be considered for nutritional support guidelines in clinical management of trauma patients, including route, time, site, formula, monitoring time, and types of nutritional support (Jacobs et al., 2004). For instance, early enteral feeding has been associated with improved outcomes; however, the effectiveness of the intervention may vary depending on the mode of feeding.

Nasogastric feeding tubes have been associated with increased incidence of pneumonia, while theoretically, feeding tubes placed more remotely decrease the risk. Gastronomies are proven to be a safe and dependable process used to provide enteral access for meeting nutritional needs of individuals with ABI and delivering essential medications (Harbrecht et al., 1998). It is suggested that having more selective guidline and specific criteria in trauma centers may result in lower rate of unnecessary tube feeding and subsequently less complications (Marcotte et al., 2018).

TABLE 15 | Administration Strategies for Nutritional Management Post ABI

Author Year Country Study Design Sample Size	Methods	Outcome
Marcotte et al. (2018) USA Cohort N = 500	**Population:** *Preselective Group (N=257)*: Mean Age= 50±21y; Gender: Male=71%, Female=29%; Mean Time Post Injury= within 24 hours; Mean GCS=10±5. *Postselective Group (N=244):* Mean age= 51±21; Gender: Male=78%, Female=22%; Mean Time Post Injury= within 24 hours; Mean GCS= 9±5. **Intervention:** Retrospective review of participants on an intensive care unit before and after a Surgical Feeding Tube (SFT) placement strategy was implemented in 2011. Participants before 2011 (2007 – 2010) were placed in the preselective group, and participants from 2012-2016 were placed in the postselective group. **Outcome Measures:** Percentage of unnecessary SFT placements, predictors of necessary SFT placement, and overall complication rates.	1. The percentage of unnecessary SFTs was significantly different between groups ($p<0.0001$) showing a decrease from 25% preselective to 8% postselective. 2. Significant predictors of necessary SFT placement were increasing age ($p<0.0001$), head injury ($p<0.0001$), cervical spinal cord injury ($p<0.0109$), and need for tracheostomy ($p<0.0001$). 3. Overall complication rate was not significantly different between the preselective and postselective groups ($p=0.2574$).

Discussion

One study examined the outcomes after placing a new administration strategy for nutritional support in a trauma center. They found that after implementation of a new Surgical Feeding Tube (SFT) placement strategy, the percentage of unnecessary SFTs significantly decreased from 25% to 8% (Marcotte et al., 2018). In addition, significant predictors of necessary SFTs were identified and included increasing age, head injury, cervical spinal cord injury and need for a tracheostomy.

Conclusions

There is level 2 evidence (Marcotte et al., 2018) that a specific surgical feeding tube placement strategy can reduce the number of unnecessary surgical feeding tube placements and subsequent complications in individuals post ABI.

KEY POINTS

- Selective surgical feeding tube placement strategies can reduce the number of unnecessary surgical feeding tubes and subsequent complications post-ABI.

Enhanced Feeding Solutions

Enhanced EN protocols are one of the strategies developed to increase the delivery of nutrition in critically ill patients, including severe ABI, based on the patients' needs. Studies showed that different enhanced EN protocols showed both beneficial and compromised outcomes (Krenitsky, 2018). For instance, EN feeding solutions enriched with immune-enhancing nutrients may decrease the occurrence of sepsis and reduce the inflammatory response.

Theoretically, glutamine is thought to enhance gut mucosal and immune cell function through its antioxidant properties, while probiotic bacteria could favorably alter the intraluminal environment, competing for nutrients and adhesion sites with pathogenic bacteria. These co-operative actions may reduce the rate of bacterial translocation and, thus, decrease both the incidence of infection and the length of hospitalization (Falcão de Arruda & de Aguilar-Nascimento, 2004).

TABLE 16 | Enhanced Enteral Nutrition for Nutritional Management Post ABI

Author Year Country Study Design Sample Size	Methods	Outcome
Wan et al. (2020) China RCT PEDro=6 N=76	**Population:** TBI=76; *Intervention Group* (n=38); Mean Age=35.97±13.12yr; Gender: Male=19, Female=19; Mean Time Post Injury=Not Reported; Severity: Mean GCS=5.47±1.59. *Control Group* (n=38); Mean Age=38.65±11.26yr; Gender: Male=17, Female=21; Mean Time Post Injury=Not Reported; Severity: Mean GCS=5.79±1.74. **Intervention:** Participants were randomized to received either probiotics (6 tablets, twice daily for 15d) along with standard enteral nutrition as	1. Serum levels of inflammatory factors gradually decreased with increasing treatment time in both groups. However, ET-1 at 15 days, and interleukin (IL)-6, IL-10, tumor necrosis factor (TNF)-α, and CRP at 7 and 15 days decreased significantly more in the intervention group (p<.05). 2. Hospitalization duration and pulmonary infection rates were significantly reduced in

Author Year Country Study Design Sample Size	Methods	Outcome
	intervention or only standard enteral nutrition as the control group. Outcome measures were assessed at baseline and the end of the intervention. **Outcome Measures:** Interleukin-6 (IL)-6, Interleukin 10 (IL-10), Tumour necrosis factor (TNF-α), ET-1, and C-Reactive protein (CRP), Glasgow Coma Scale (GCS), Sequential Organ Failure Score (SOFA), Acute Physiology and Chronic Health Evaluation-II (APACHE-II), Mortality.	the intervention group compared to the control group (p<.001). 3. GCS scores at 15 days were significantly lower in the intervention group compared with the control group (p<.001). 4. There was no significant difference in 1-month mortality rates, intracranial, incision, or blood infection rates, sepsis, septic shock, or systemic inflammatory response syndrome between the two groups (p>.05)
Wandrag et al. (2019) UK RCT PEDro=4 N=8	**Population:** TBI; *Intervention Group* (n=4); Mean Age=53yr; Gender: Male=4, Female=0; Time Post Injury=Not Reported; Mean ISS=27, Mean GCS=Not reported. *Control Group* (n=4); Mean Age=60yr, Gender: Male=2, Female=2; Time Post Injury=Not Reported; Mean ISS=42, Mean GCS=Not reported. **Intervention:** The intervention group received 5 g Leucine-enriched essential amino acid (L-EAA) 5x/day in addition to standard feed for up to 14d. The control group received standard feed only. **Outcome Measures:** C-reactive protein (CRP), Albumin levels, Interleukin (IL)-6, Interleukin IL-10 levels, Nitrogen Balance, Barthel Index (BI), Katz Index of Independence in Activities of Daily Living, Medical Research Council (MRC) Score	1. L-EAA doses were provided on 91/124 (73%) occasions. 2. All of the required inflammatory and urinary marker data were collected, meeting the >90% target. 3. Serial muscle depth measurements were lacking (50% measurements completed, lower than the >90% target) due to short length of stay. 4. Protein turnover studies were performed on five occasions. 5. Manual strength testing (MRC sum score) could not be performed as participants were not able to respond to the screening questions. 6. The Katz and Barthel indices remained at zero for all participants throughout the study. 7. L-EAA supplement doses were deliverable 73% of the time, higher than the 70% target.
Jia et al. (2018) China RCT PEDro=8 N=62	**Population:** Severe TBI; *Observational Group (N=34)*: Mean Age=41.5±10.8y; Gender: Male=22, Female= 12; Mean Time Post Injury= within 24 hours; Mean GCS=5.5±1.3. *Control Group (N=28):* Mean Age= 45.4±9.6y Gender: Male=17, Female=11; Mean Time Post Injury= within 24 hours; Mean GCS=6.2±0.7. **Intervention:** Both groups received Enteral Nutrition (EN) upon admission. Participants were randomized into 1 of two groups. The observational group was given sequential nutritional support. This was based on a participants' energy needs and tolerance. Different solutions were used over the course of their first 3 days in intervention, starting with pepsin short peptide type EN moving toward a typical whole protein method. The control group was given standard enteral nutritional formula for their nutrition requirements.	1. ALB and TP were significantly higher in the observational group than in the control group on day 14 (p<0.05). 2. Hs-CRP levels were significantly lower in observational group than the control group on day 7 (p=0.015) and 14 (p=0.047). 3. NSE levels were significantly lower in the observational group than the control group on day 14 (p=0.012). 4. GCS scores were significantly higher in the observational group on day 14 (p<0.05). 5. The percentage of regulatory T cells in peripheral lymphocytes and in the CD4 lymphocytes were significantly lower in the observational group on day 7 (p<0.05) and day 14 (p<0.01). percentages.

Author Year Country Study Design Sample Size	Methods	Outcome
	Patients were assessed on their first day, 7th day, and 14th day. **Outcome measures:** Albumin (ALB), total protein (TP), high-sensitivity C-reactive protein (Hs-CRP), neuron specific enolase (NSE), Glasgow Coma Score (GCS), and percentage of CD4-CD25 regulatory T cells in peripheral lymphocytes and CD4-CD25-CD127dim T cells in the CD4 lymphocytes.	
Falcao de Arruda & Aguilar-Nascimento (2004) Brazil RCT PEDro=7 N=20	**Population:** TBI; *Intervention Group* (n=10); Mean Age=27 yr; Gender: Male=10, Female=0; Mean GCS Score=7; *Control Group* (n=10); Mean Age=26 yr; Gender: Male=9, Female=1; Mean GCS Score=7. **Intervention:** Participants were randomized to receive either the standard enteral feeding (EN) diet (control) or the glutamine- and probiotics-enhanced EN diet (intervention group). **Outcome Measures:** Incidence of infection, Length of Stay (LOS) in ICU, ventilation days.	1. Infection rate was higher in the control than in the intervention group (p=0.03). 2. LOS (p<0.01), as well as the number of days on ventilation (p=0.04), was significantly higher in the control group compared to the intervention group.
Taylor et al. (1999) UK RCT PEDro=4 N=82	**Population:** TBI; *Intervention Group (n=41)*: Median Age=34 yr, Gender=Not reported, Median Best GCS Score=9. *Control Group (n=41):* Median Age=28 yr, Gender=Not reported, Median Best GCS Score=8. **Intervention:** Participants were randomly allocated to receive either the standard enteral nutrition (EN) or the enhanced EN (intervention). EN was initiated from day 1 in both groups. In the control group, EN was gradually increased from 15 mL/hr up to estimated energy and nitrogen requirements. In the intervention group, feeding was administered at a rate that met estimated energy and nitrogen requirements. Follow-up at 3 and 6 mo. **Outcome Measures:** Serum concentrations of albumin, pre-albumin, C-reactive protein (CRP), α1-acid glycoprotein (AGP), Insulin-like Growth Factor (IGF-1), Glasgow Coma Scale (GCS), Glasgow Outcome Scale (GOS), Injury Severity Score (ISS), Acute Physiology and Chronic Health Evaluation-II (APACHE-II)	1. Participants receiving enhanced EN had a significantly higher mean percentage of energy (p=0.0008) and nitrogen (p<0.0001) requirements met over the initial week following injury when compared to the control group. This finding was mostly attributable to improved NG feeding as only 14 intervention participants (34%) had intestinal tubes successfully placed. 2. The median percentage of energy and nitrogen requirements delivered in control participants remained <60% even by day 7 post injury. 3. Neurologic outcome at 6 mo follow-up (intervention, 68% versus control, 61%; p=0.64) was similar between the groups, but there was a trend toward improved outcome at 3 mo follow-up in favour of the intervention group (61% versus 39%; p=0.08). 4. Intervention participants had lower rate of infections (61% versus 85%; p=0.02) and earlier discharge (p=0.008). 5. Enhanced EN was associated with a reduction in the ratio of serum concentration of CRP/ALB up to day 6 after injury (p= .004).

Author Year Country Study Design Sample Size	Methods	Outcome
Buckley et al. (2021) USA Case Series N=51	**Population:** Severe TBI; N=51, Mean Age=41±17yr; Gender: Male=39, Female=12; Mean GCS=7±4. **Intervention:** A modified EN regimen was administrated for ICU-admitted TBI Individuals who were on propofol therapy. The modify EN regimen included isocaloric (1-1.06kcal/mL) high protein formula (64g/L) and standard protein formula (44g/L) with concurrent liquid protein boluses. Actual protein intake was compared with projected protein intakes from high protein content and standard protein content enteral formulas when given at an isocaloric intake. **Outcome Measures:** Average daily caloric intake, average daily protein intake.	1. Average caloric intake from propofol was 5±3 kcal/kg/d (range, <1–15 kcal/kg/d). 2. Daily EN caloric intake ranged from 7 ± 4 kcal/kg/d (day 2) to 16±9 kcal/kg/d (day 5; p<.001). 3. Average protein intake ranged from 0.6±0.4 g/kg/d (day 2) to 1.5±0.7 g/kg/d (day 5; P < .001). 4. The modified EN regimen resulted in daily delivery of 24%-38% more protein than a high protein content formula and 2x as much protein than the standard protein content formula (p<.001).
Painter et al. (2015) USA Cohort N=240	**Population:** Severe TBI; *Immune Enhancing Nutrition (Li et al.) Group (n=126)*: Mean Age=43.7yr; Gender=Not reported; Mean GSC=6; *Standard Formula (Kostadima et al.) Group (n=114)*: Mean Age=46.7yr; Gender=Not reported; Mean GCS=7. **Intervention:** Retrospective analysis of data from people with severe TBI who received either IEN enteral feeding or standard enteral feeding to understand if IEN provide better outcomes. **Outcome Measures:** Hospital and ICU Length of Stay (LOS), cultures of blood, urine, and respiratory, temperature, white blood cell (WBC) count, chest X-Ray, nutrition type and measures.	1. IEN had longer LOS in ICU (p=0.02) and more days on ventilator (p=0.001) than SF but were less likely to have bacteremia (p<0.05). 2. No significant difference between IEN and SF in rates of urinary tract infections (p=0.48), Clostridium difficile (p=0.63), and pneumonia (p=0.89). 3. Similar fungi/bacteria present within both groups. 4. No significant difference in mortality rates during hospital stay (p=0.88).

Discussion

A RCT comparing standard diet to glutamine and probiotic enhanced diet in individuals with brain injury showed lower infection rates in the enhanced diet group, as well as decreased length of stay (LOS) and ventilator days for those on enhanced diets (Falcao de Arruda & de Aguilar-Nascimento, 2004). Another RCT examined the impact of probiotics combined with EN on endothelin-1 and C-reactive protein levels, as well as prognosis in individuals with severe TBI. The findings revealed that while serum levels of inflammatory factors decreased with increasing treatment time in the combined treatment group and control group that received EN alone, serum levels of ET-1, CRP, and IL-6, IL-10, and TNF-alpha reduced significantly more in the combined treatment group participants. In addition, compared to the control group, the combined treatment group had shorter length of hospital stay, lower rates of pulmonary infection, and greater improvement GCS following the intervention. The authors concluded that probiotics combined with EN may facilitate recovery in participants with severe TBI (Wan et al., 2020).

Findings from these two studies are in line with the results of a systematic review concerning participants with severe craniocerebral Injury, which suggested that probiotics supplementation combined with EN could decrease the risks of infection, mortality, and gastrointestinal complications, and may shorten the length of hospital stay (Du et al., 2020).

Painter et al. (2015) reviewed participants given either immune enhancing nutrition or standard formula. Surprisingly, patients with IEN had longer LOS in ICU and more days on ventilator than SF but were less likely to have bacteremia (Painter et al., 2015). This conflicts with two other RCTs, one of which found that enhanced EN feeding resulted in earlier discharge and fewer infections in patients with ABI (Taylor et al., 1999). Taylor et al. (1999) also found that those receiving enhanced EN, compared to standard EN, met significantly more of their daily nitrogen and energy requirements. The other RCT by Jia et al. (2018), it was found that sequential enhanced enteral feeding resulted in significantly higher protein levels and GCS scores 14 days post-treatment (Jia et al., 2018).

Leucine-enriched essential amino acid (L-EAA) supplementation has been shown to improve nutritional status and muscle function in elderly institutionalised individuals (Anthony et al., 2001). Research regarding its effectiveness in facilitating recovery in patients with ABI is limited. One study has explored the feasibility of delivering L-EAA to mechanically ventilated trauma patients, including those with TBI, and found that while administering L-EAA to patients with TIB may be feasible, there are significant barriers to measurement of the intervention outcomes (Wandrag et al., 2019).

Patients in ICU need different treatment regimens and the medications may affect the balance of energy and change their nutritional needs. Buckley et al. (2021) discussed that TBI patients on propofol therapy in ICU have extra energy intake from this medication and subsequently need lower numbers of calories while they still need the same amount of protein, and this conflict may result in overfeeding of patients to provide the needed protein (Buckley et al., 2021). They examined isocaloric protein enhanced EN regimens and suggested that the protein-enhanced EN regimen could supply the required protein for patients without overfeeding.

Individuals with brain injury have higher energy and protein expenditures and are prone to infections, thus supplementing diet and enhancing feeding solutions may be a feasible option to consider when improving outcomes.

Conclusions

There is level 1b evidence (Wan et al., 2020) that probiotics combined with early enteral nutrition may reduce serum levels of ET-1, CRP, and IL-6, IL-10, and TNF-α and facilitate recovery in patients with severe TBI.

There is level 2 evidence (Wandrag et al., 2019) that although administering Leucine-enriched essential amino acid to patients with TBI may be feasible, there are significant barriers to measurement of the intervention outcomes.

There is level 1b evidence (Jia et al., 2018) that sequential enhanced enteral feeding may increase protein levels and GCS scores 14 days post-treatment in patients post ABI.

There is level 1b evidence (Falcao de Arruda & Aguilar-Nascimento, 2004) that glutamine- and probiotics-enhanced diet may reduce infection rates, length of stay, and ventilator days compared to standard diet in patients post TBI.

There is level 2 evidence (Taylor et al., 1999) that enhanced enteral feeding may result in higher energy and nitrogen requirements compared to standard enteral feeding, but fewer infections and earlier discharge in patients post head injury.

There is level 4 evidence (Buckley et al., 2021) that protein-enhanced EN regimen could improve the protein intake without any increase in the calory intakes in patients on propofol therapy.

There is level 2 evidence (Painter et al., 2015) that immune enhancing nutrition may result in longer length of stay and ventilator days compared to standard formula, but lower risk of bacteremia in patients post TBI.

KEY POINTS

-Immune-enhanced EN regimens may result in lower rates of inflammation and infection, and better recovery. However, there is conflicting evidence as to whether immune enhanced EN solutions reduce ventilator dependency, and hospital length of stay in patients post-ABI.
-Protein-enhanced EN regimens may be helpful for those who have elevated protein needs but lower caloric needs.

Metoclopramide

Individuals who sustain a severe TBI often show signs of gastroparesis. For many individuals with a severe ABI, their energy requirements may reach 60% more than predicted. Metoclopramide has been used and continues to be used to enhance the effectiveness of enteral nutrition, despite its limited success and the inconsistent findings supporting its use (Nursal et al., 2007).

TABLE 17 | Metoclopramide and Enteral Nutrition for Nutritional Management Post ABI

Author Year Country Study Design Sample Size	Methods	Outcome
Nursal et al. (2007) USA RCT PEDro=9 N=19	**Population:** TBI; *Intervention Group (n=10*): Mean Age=43.8 yr; Gender: Male=8, Female=2; Mean GCS Score=7.7. *Control Group (n=9):* Mean Age=43 yr; Gender: Male=8, Female=1; Mean GCS Score=8.9. **Intervention:** Participants in the intervention group were administered 10 mg (2 mL) IV metoclopramide 3x/day for 5 days. The control group received the same volume of control saline solution for the same duration. **Outcome Measures:** Paracetamol absorption test, amount of calories supplied, intolerance and/or complication rates.	1. Amount of oral/enteral calories in relation to the total number of calories received during the first 5 days was higher for those in the control group (p=0.043). 2. There were no differences between the groups in both feeding intolerance and complication rates (p=0.543 and p=0.930, respectively). 3. There was no significant difference between the groups when looking at the results of the paracetamol absorption test. 4. When looking at absorption parameters, those in the intervention group had levels that were slightly more pronounced than those in the control group.

Discussion

A single RCT by Nursal et al. (2007) compared an intervention group receiving 10 mg of metoclopramide per day for five days to a control group receiving placebo. All patients were receiving EN through a nasogastric feeding tube. When looking at the absorption parameters of the two groups, a small non-significant difference was found, with the levels in the intervention group being slightly more pronounced. Overall, the study showed no advantages of metoclopramide in a TBI population.

Conclusions

There is level 1b evidence (Nursal et al., 2007) that metoclopramide may not be effective compared to placebo for gastric emptying in patients post TBI.

KEY POINTS

- The use of metoclopramide to aid in gastric emptying may not be effective in individuals with TBI.

Total Parenteral Nutrition

Total Parenteral Nutrition (TPN) provides complete nutrition intravenously. Usually, TPN is initiated when a person's stomach or bowel is not functioning properly (American Society for Parenteral and Enteral Nutrition, 2018). TPN feeding solution includes all essential vitamins and minerals, as well as protein, carbohydrates, fats, and electrolytes (Mousavi et al., 2014). If a patient requires TPN to meet

their nutritional and caloric requirements, it is essential to initiate TPN as quickly as possible, as a delay in nutrition can result in severe complications, delayed discharge, and longer rehabilitation stays.

TABLE 18 | Parenteral Nutrition for Nutritional Management Post ABI

Author Year Country Study Design Sample Size	Methods	Outcome
Mousavi et al. (2014) Iran RCT PEDro=6 N=26	**Population:** TBI; *Intervention Group (n=13):* Mean Age=31yr; Gender: Male=13, Female=0; Mean GCS Score=7.3. *Control Group (n=13):* Mean age=36.6yr; Gender: Male=13, Female=0; Mean GCS Score=8.4. **Intervention:** Participants on parenteral nutrition were randomly allocated to receive continuous infusion of 50 IU insulin (Intensive Insulin Therapy; IIT) or conventional glucose treatment (CGC; control). IIT group had Blood Glucose (BG) levels maintained at 80 mg/dl–120 mg/dl. Participants were followed up on day 7 and 14**.** **Outcome Measures:** Occurrence of hypoglycemic episodes, Blood Glucose (BG) concentration, Arm Circumference, C-Reactive Protein (CRP), Cholesterol Levels, Triglycerides levels, Bilirubin levels, Lactate dehydrogenase (LDH), Magnesium levels, Phosphorus levels, Chloride levels.	1. Mean BG concentration was significantly lower in the IIT group compared to the CGC group (118±28 mg/dl versus 210±31 mg/dl; p<0.01). The CGC group had more hyperglycemic episodes. 2. There were no significant between group differences in any of the secondary outcome measures on day 7 follow-up (p>0.05). 3. On day 14, the IIT group had significantly lower levels of CRP (p=0.0001), triglycerides (p=0.02), magnesium (p=0.03), and phosphorus (p=0.01). 4. Chloride levels were significantly elevated in IIT patients compared to CGC patients (p=0.02). These changes were largely in accordance with the hormonal effects of insulin.
Justo Meirelles & de-Aguilar-Nascimento (2011) Brazil RCT PEDro=5 N=22	**Population:** TBI; *Enteral Nutrition (EN) Group*: Mean Age=31 yr; Gender: Male=11, Female=1; Mean GCS Score=9. *Parenteral Nutrition (TPN) Group*: Mean Age=31 yr; Gender: Male=9, Female=1; Mean GCS Score=9. **Intervention:** Patients were randomized to receive either EN or TPN. Both groups received a 25-30 kcal/kg/day and 1.5 g/kg/day of protein. EN was administered via 8 or 10F oro- or naso-enteral feeding tube in gastric position with pump infusion. TPN was administered via central venous access. Patients assessed daily for 5 days. **Outcome Measures:** Mortality, morbidity, ICU Length of Stay (LOS), days of mechanical ventilation, amount of calories and protein received/d, blood glucose, albumin, urea, creatinine, C-Reactive Protein (CRP), urinary urea (N).	1. No significant differences were found in morbidity and mean ICU LOS between the EN and TPN groups. 2. The mean serum glucose level in TPN group was significantly higher than EN group (p<0.001) 3. A progressive caloric deficit occurred in both groups (p=0.001) without any between group difference, despite the everyday increase in the number of calories. 4. Nitrogen was delivered more efficiently in TPN group than EN group, and TPN group received higher amounts of nitrogen than the NE group (p < 0.05). 5. There was a trend (p = 0.06) of 24 h urinary N loss to be greater in TPN group; however, both groups showed similar significant improvements (p=0.001) in the nitrogen balance as a result of nutritional therapy.

Author Year Country Study Design Sample Size	Methods	Outcome
Nataloni et al. (1999) Italy RCT PEDro=4 N=45	**Population:** Head injury; N=45, Gender: Male=31, Female=14. *Group A (n=15)*: Mean Age=45.6yr, Mean GCS Score=6. *Group B (n=15)*: Mean Age=46.3yr, Mean GCS Score=6. *Group C (n=15)*: Mean Age=44.2yr, Mean GCS Score=5. **Intervention:** Patients were randomly administered one of the following feeding conditions: enteral (Group A), parenteral (Group B), or both enteral and parenteral (Group C). Those who participated were expected to stay in ICU for ≥3 days. Feeding began within 2 days of ICU admission and continued for the length of stay. **Outcome Measures:** Serum pre-albumin, Retinol-Binding Protein (RBP), nitrogen balance. Assessments were made at baseline and after (day 3, 7 and 11).	1. Nitrogen balance, which was negative for all groups, improved over the course of treatment; however, it only significantly improved in Group A by day 11 ($p<0.0001$). 2. Pre-albumin and RBP significantly increased in all groups, and the increase was significantly greater in Group A compared to both Group B ($p<0.001$) and Group C ($p<0.01$). 3. Significant differences in the level of pre-albumin began at day 3 ($p<0.01$) while the differences in the level of RBP began at day 7 ($p<0.01$).
Adolph et al. (1995) Germany RCT PEDro=6 N=24	**Population:** Severe Head Injury; *CH Group* (n=12); Mean Age=30±16yr; Gender: Male=12, Female=0; GCS Range=4-6. *CH+MCT/LCT Group* (n=12); Mean Age=32±13yr; Gender: Male=12, Female=0; Mean GCS=4-6. **Intervention:** Participants were randomized to receive either carbohydrate as the sole energy source (CH TPN regimen) or combined TPN regimen of CH plus medium-chain triglyceride/long-chain triglyceride (CH+MCT/LCT) for 8 days. The levels of lipid and carbohydrate in these two isocaloric isonitrogenous TPN regimens were compared. **Outcome Measures:** Triglyceride (TG) Concentration, Serum Phospholipid Fatty Acid Patterns, Glucose Level.	1. Serum TB concentration increased for both groups over the study period, but there was no significant difference in the TG level between groups on the last 2 days. 2. The pattern of saturated fatty acids did not change over the study for both groups, however, there was a tendency to elevated monounsaturated fatty acids in CH group compared to the other group on the day7 ($p<0.005$). 3. In CH group, linolenic acid and α-linolenic acid deficiency, and compensatory increase of nonessential N-9 fatty acids were observed. 4. Arachnoid acid declined for both groups throughout the study. 5. There was no fatty acid pattern imbalance in the combined TPN group. 6. Both groups showed minor increases in glucose levels during the study.
Borzotta et al. (1994) USA RCT PEDro=4 N=49	**Population:** TBI; Gender: Male=40, Female=9; *Early Parenteral Nutrition (TPN) Group (n=21):* Mean Age=28.9 yr; Mean GCS Score=5.4. *Enteral Nutrition (ENT) Group (n=27):* Mean Age=26.2 yr; Mean GCS Score=5.2. **Intervention:** Participants were randomized to either early TPN or ENT. TPN tapering was began at day 5 for converting to gastric feeding. The ENT group had enteral feeding through jejunal tubes. Assessments made daily for 10 days and weekly for 5wk thereafter.	1. No significant differences noted for nitrogen excretion or balance, energy expenditures, meeting nutritional goals, and frequency of infections. 2. Patient complications such as hyperglycemia ($p<0.05$) and diarrhea ($p<0.05$) were more common among patients receiving TPN. 3. Efficiency of feeding, measured by ratio of calories to MREE, showed an advantage for TPN at day 3, but none after.

Author Year Country Study Design Sample Size	Methods	Outcome
	Outcome Measures: Measured Energy Expenditure (MEE), Nitrogen Balance, Serum Transferrin levels, Serum Bilirubin, Serum Albumin, Serum Gamma Glutamyl-Transferase, Incidence of Infection.	4. There were no differences in mortality at the end of follow-up.
Young et al. (1987) USA RCT PEDro=5 N=96	Population: Severe TBI; Total Parenteral nutrition (TPN) Group: Mean Age=29.9 yr, Gender=Not reported, Peak Admission 24-hour GCS Score=6.7±0.34. Enteral feeding (EN) Group: Mean Age=33.8 yr, Gender=Not reported, Peak Admission 24-hour GCS Score=6.8±0.62. Intervention: Patients were randomly assigned to receive either TPN or EN. TPN was initiated within 48 hr post-injury. EN was initiated when tolerated by patients. Study went from admission to day 18. Assessments made every 6 hr in the ICU, or 1x/day in the hospital ward. Outcome Measures: Intracranial pressure (ICP), serum glucose levels.	1. No Significant differences were found between groups in peak daily ICP; ICP was >20 mmHG in 75% of the TPN patients and 73% of the EN patients. 2. Standard therapy was ineffective in controlling elevated ICP in 36% of the TPN and in 38% of the EN group. 3. There were no significant between-group differences in serum osmolality. 4. For the first 12 days, the TPN group received more calories and protein than the EN group (p=0.0001). 5. There was a significant day × nutrition group interaction (p<0.0001); serum glucose levels were higher in the TPN group for the first 13 days post injury than EN group who had increased mean serum glucose content after 13 days.
Hadley et al. (1986) USA RCT PEDro=4 N=45	**Population:** TBI; N=35, Total Population Median Age=28yr. *TPN group (n=24)*: Mean Age=Not reported, Gender: Male=22, Female=2, Mean Admission GCS=5.8. *EN group (n=21)*: Mean Age=Not reported, Gender: Male=18, Female=3, Mean Admission GCS=5.9. **Intervention:** Patients were randomly assigned to receive either Total Parenteral Nutrition (TP) or enteral nutrition (EN). Patients received high nitrogen and calorie feedings for a 14-day period of the study to try to obtain a positive nitrogen and calorie balance. Nitrogen loss was measured every other day. **Outcome Measure:** Urinary nitrogen levels.	1. Patients who received TPN achieved significantly higher mean daily nitrogen intakes (p<0.01) and losses (p<0.001) compared to those who received EN. 2. There was no significant between-group difference in nitrogen balance.
Hausmann et al. (1985) Germany RCT PEDro=4 N=20	**Population:** TBI; Gender: Male=20, Female=0; *Total parenteral nutrition (TPN) Group* (n=10); Age Range=15-38; Median GCS=6 (range 5-7). *Combined enteral-parenteral nutrition (CN) Group* (n=10); Age Range=19-48; Median GCS=6 (range 5-7). **Intervention:** Patients were randomly assigned to one of the following feeding regimes: Total Parenteral Nutrition (TPN) or the Combined enteral-parenteral Nutrition (CN). All received maximal glucose intake of 500 g/day and sorbitol of 100 g/d. Parenteral nutrition was administered continuously via a central venous	1. There was no significant difference in mortality between the TPN and CN groups (40% vs 20%). 2. Up to day 7, the quantity of regurgitated gastric fluid was significantly lower in the TPN group compared to the CN group (p<0.05). 3. Protein concentration of the reflux fluid in the CN group (1.1-4.2 g/dl) was significantly elevated compared to the TPN group (0.53-0.84 g/dl) (p<0.05).

Author Year Country Study Design Sample Size	Methods	Outcome
	line over 24 hr. Enteral feeding was administered through a nasogastric tube at 2 hr intervals. Daily fluid balance was corrected with electrolyte solutions or diuretics. Patients were assessed up to 8 days post injury. **Outcome Measures:** Mortality, Negative Nitrogen Balance (NNB), Protein Concentration of gastric reflux fluid.	4. NNB could not be reached in groups and there were no statistically significant differences in NNB between groups.
Rapp et al. (1983) USA RCT PEDro=4 N=38	**Population:** Head injury; Standard Enteral Nutrition (SEN) Group (n=18): Mean Age=34.9 yr; Gender=Not Reported; Mean GCS Score=7.2. Total Parenteral Nutrition (TPN) Group (n=20): Mean Age=29.2 yr; Gender=Not Reported; Mean GCS Score=7.7. **Intervention:** Patients were randomly assigned to either the SEN or TPN group. TPN therapy was initiated within 48 hr of admission. EN was given via nasogastric tubes and initiated when tolerated. **Outcome Measures:** Glasgow Coma Scale (GCS), Mortality, Serum Transferrin Levels, Albumin Levels, Calorie Intake, Nitrogen balance, Serum glucose levels.	1. No baseline between-group differences except for mean peak temperature during the first 24hr of hospitalization; TPN group had a higher mean temperature than SEN group (38.6ºC versus 38.0oC; p=0.02). 2. Within the 18-day period, 8 of the 18 patients died in the SEN group compared to 0 deaths in the TPN group (p<0.0001). 3. The TPN group had a significantly greater mean intake in nitrogen/d then the SEN group (10.2 gm versus 4.0 gm; p=0.002); the overall nitrogen balance was also significantly different between groups (p=0.002). 4. No significant between group difference was found in serum albumin levels over time.
Fan et al. (2016) China PCT N=40	**Population:** Severe TBI, N=120, Total Population Mean Age=41.69yr; Gender: Male=62, Female=58. GCS Range=6-8 **Intervention:** Participants were assigned to receive nutrition Enterally (EN) (n=40), Parenterally (PN) (n=40), or combined (EN+PN) (n=40), supported by nutritional therapies. Measures were taken at day 1 and day 20. **Outcome Measures:** Levels of lymphocytes and Immunoglobulins, Serum Total Protein, Albumin, Pre-albumin, Hemoglobin, Complication Occurrence Rate, Length of Stay (LOS), Mortality rate.	1. Total serum protein was significantly decreased in the PN group (p<0.01) compared to serum protein on day 1, whereas total serum protein was significantly increased in EN and EN+PN groups (p<0.01). 2. The EN group had significantly higher rates of diarrhea (p<0.01) compared to the PN and EN+PN group. 3. Stress ulcers were significantly higher in the PN group (p<0.01) than the other two groups. 4. The EN group had significantly higher rates of aspirated pneumonia (p<0.01). The EN group had the lowest rates of pyemia (p<0.01). 5. The EN+PN group had the lowest rates of hypoproteinemia (p<0.01) and intracranial infection (p<0.01).

Discussion

Fan et al. (2016) conducted a prospective controlled trial comparing EN versus PN versus combined EN and PN. Total serum protein, prealbumin, and hemoglobin were significantly decreased in the PN group ($p<0.01$), which corresponds to a degradation in nutritional status; in the EN and EN+PN groups, total serum and protein levels significantly increased ($p<0.01$) after nutritional treatment. Therefore, the authors suggest a combination of EN+PN to improve prognosis and nutritional status for patients post injury.

A RCT assessing the effect of glycemic control on PN complications in hospitalized patients with brain injury demonstrated that treatment using an insulin infusion significantly decreased blood glucose levels when compared to a conventional glucose treatment (Mousavi et al., 2014). The experimental group also had significantly lower concentrations of C-reactive protein and triglycerides compared to the control group (Mousavi et al., 2014). The study authors concluded that although more research is needed, insulin infusions improved some parenteral nutrition complications (Mousavi et al., 2014).

With respect to nitrogen balance, Justo Meirelles and de Aguilar-Nascimento (2011) also evaluated the effects of EN and PN in 22 patients with moderately severe TBI and found that parenteral nutrition delivered nitrogen more effectively. Both groups received increasing quantities of nitrogen each day, with those in the total parenteral nutrition (TPN) group receiving significantly more. Despite the increased daily loss of nitrogen, all patients showed significant improvement in nitrogen balance as a result of nutritional therapy (Justo Meirelles & de Aguilar-Nascimento, 2011). Nataloni et al. (1999) studied the effects of EN, PN, or both in a group of patients with ABI while in the intensive care unit. Even though there was a negative nitrogen balance in all groups, all showed improvement over the course of the study, however a positive nitrogen balance was only seen in the enteral group. Furthermore, other studies have found no difference in nitrogen balance between PN and EN (Borzotta et al., 1994; Hadley et al., 1986; Hausmann et al., 1985).

Young et al. (1987) investigated the effects of TPN versus EN administration on intracranial pressure (ICP) levels in 95 individuals with severe brain injury. Participants were randomly assigned to receive TPN or EN and ICP pressure was monitored, as well as serum glucose levels and hyperosmolality. No significant differences were observed between groups in relation to ICP levels or hyperosmolality, suggesting that EN and TPN can be administered safely to individuals with severe brain injury without causing serum hyperosmolality or affecting ICP therapy.

Hausmann et al. (1985) conducted a RCT to investigate the effects of combined EN and PN compared to TPN on protein catabolism. Findings from the study noted a difference in nitrogen balance between the two feeding regimes, however, these differences were not significant. The combination (EN and PN) group did have significantly higher protein concentrations compared to the TPN group. Although, no

other relevant differences in the metabolic data or mortality between each of these intervention groups was found (Hausmann et al., 1985).

Conclusions

There is level 1b evidence (Mousavi et al., 2014) that insulin infusions significantly decrease blood glucose levels in patients post TBI.

There is level 1b evidence (Adolph et al., 1995) that using carbohydrate as the only source of energy in TPN regimens results in fatty acids deficiency.

There is level 2 evidence (Justo Meirelles & de-Aguilar-Nascimento, 2011) that TPN delivered nitrogen more efficiently than EN therapy in patients post TBI. However, both groups showed a significant improvement in nitrogen balance as a result of nutritional therapy.

There is level 2 evidence (Nataloni et al., 1999) that EN may be effective for improving nitrogen balance compared to PN and EN plus PN in patients post head injury.

There is level 2 evidence (Borzotta et al., 1994) that patients post closed head injury treated with TPN or EN had no differences in nitrogen balance, energy expenditures, meeting nutritional goals and frequency of infections. However, EN may lead to decreased rates of hyperglycemia and diarrhea compared to PN.

There is level 2 evidence (Young et al., 1987) that ICP and serum osmolality are not affected by TPN or EN interventions in patients post severe head injury.

There is level 2 evidence (Hadley et al., 1986) that patients post TBI receiving NG or TPN had no significant changes in nitrogen balance, although, NG may be more effective in reducing nitrogen intake and nitrogen loss, when compared to TPN.

There is level 2 evidence (Hausmann et al., 1985) that parenteral nutrition reduces the amount of regurgitated gastric fluid compared to combined EN+PN, however, nitrogen balance could not be reached for either PN or combined EN and PN in patients post ABI.

There is level 2 evidence (Rapp et al., 1983) that EN may reduce mean intake of nitrogen compared to PN in patients post head injury.

There is level 2 evidence (Fan et al., 2016) that EN may increase serum protein, the rate of aspirated pneumonia and diarrhea when compared to PN or combined EN+PN in patients post ABI.

KEY POINTS

- Parenteral nutrition (PN) with a continuous infusion of insulin may lower blood glucose levels in ABI populations.
- The evidence regarding which method of feeding (EN or PN) is optimal to deliver nitrogen, meet required energy expenditures, nutritional goals and prevent complications (e.g., diarrhea and pneumonia) is conflicting.
- Further research is needed to clarify the effect of both feeding routes on nitrogen balance post ABI.
- Using carbohydrate as the only source of energy in TPN regimen may cause fatty acids deficiency.

Timing

Early PN support provided directly following injury could assist in the maintenance of immunocompetence and help reduce the incidence of infection following ABI (Sacks et al., 1995).

TABLE 19 | Timing of Parenteral Feeding for Nutritional Management Post ABI

Author Year Country Study Design Sample Size	Methods	Outcome
Sacks et al. (1995) USA RCT PEDro=5 N=9	**Population:** Head injury; *Early PN Group (n=4)*: Mean Age=39.3 yr; Gender: Male=4, Female=0; Mean GCS Score=8. *Delayed PN Group (n=5)*: Mean Age=35.2 yr; Gender: Male=4, Female=1; Mean GCS Score=7. **Intervention:** Participants were randomly allocated to receive either early Parenteral Nutrition (PN) at day 1 or delayed PN at day 5. All participants received PN through a central venous catheter with a nutrient goal of 2 g protein/kg/d & 40 non-protein kcal/kg/day for at least the initial 14 days of hospitalization. Assessments were made on entry, and days 3, 7, and 14. **Outcome Measures:** T-lymphocytes with expression of CD4 and CD8 antigens, Lymphocyte response following Con A stimulation, Interleukin-6 (IL-6) concentrations, Pre-albumin levels.	1. From baseline to day 14, there was a significant increase in the total CD4 cell count ($p<0.05$) and in CD4 (%) ($p<0.001$) in the early PN group, while remaining relatively stable in the delayed PN group. Differences in total CD4 cell count and in CD4 (%) at day 14 was significant between the groups as well ($p<0.05$). 2. The CD4-CD8 ratio significantly increased from baseline to day 14 in the early PN group ($p<0.05$), but not in the delayed PN group. The difference between groups, however, was not significant. 3. From baseline to day 14, following Con A stimulation, an improved lymphocyte response was demonstrated in the early PN group ($p<0.05$), but not in the delayed PN group.

Discussion

A study by Sacks et al. (1995) found that in individuals with closed head injuries, early PN nutrition was beneficial in modifying immunologic function. More specifically, it aided in improving CD4 cells, CD4-CD8

ratios, and T-lymphocyte responsiveness to Con A. Further research is warranted to determine if this is a consistent effect of early versus late PN (Sacks et al., 1995).

Conclusions

There is level 2 evidence (Sacks et al., 1995) that early parenteral nutrition support may improve immunologic function compared to delayed parenteral nutrition in patients post ABI.

KEY POINTS

- Early parenteral nutrition support may improve immunologic function in individuals with ABI.

Combined Nutritional Interventions

Often times it is necessary to use both EN and PN administration strategies to ensure that an individual is meeting their caloric needs. For this reason, many studies measure their combined effect, these studies are listed below. It should be noted that, in clinical practice, optimal feeding methods should be decided by the clinician based on the patient individual needs and nutrition requirements.

TABLE 20 | Combination or Comparative Nutritional Strategies for Nutritional Management Post ABI

Author Year Country Study Design Sample Size	Methods	Outcome
Zhang et al. (2020) China RCT PEDro= 6 N=82	**Population:** Severe TBI; *Observation group (n=41):* Mean Age=64.7±6.6yr; Gender: Male=24, Female=17; Mean GCS=5.67±2.21. *Control group (n=41):* Mean Age=64.3±5.4yr; Gender: Male=26, Female=15; Mean GCS=5.42±2.39. **Intervention:** Control group was given enteral nutrition (EN) on basis of routine treatment. Observation group was given EN combined with parenteral nutrition (PN) nursing intervention. **Outcome Measures:** Hemoglobin (Ohbe et al.), Total protein (TP), Albumin (Alb), Prealbumin (Prealb), Glasgow Outcome Scale (GOS)	1. Hb, TP, Alb and Prealb levels in the observation group were significantly higher than in control ($p<0.01$) after treatment. 2. Average GOS after treatment was higher in the observation group (3.42±1.71) than in the control (2.43±1.52) ($p<0.05$). 3. The incidence of adverse reactions such as vomiting, diarrhea, abdominal distension, constipation, gastrointestinal bleeding, and lung infection in the observation group was lower than that in the control group ($P<0.05$).
Nataloni et al. (1999) Italy RCT PEDro=4 N=45	**Population:** Head injury; Mean Age=28 yr; Gender: Male=31, Female=14. *Group A (n=15)*: Mean GCS Score=6. *Group B (n=15)*: Mean GCS Score=6. *Group C (n=15)*: Mean GCS Score=5. **Intervention:** Participants were randomly administered one of the following feeding conditions: enteral (Group	1. Nitrogen balance, which was negative for all groups, improved over the course of treatment; however, it only significantly improved in Group A by day 11 ($p<0.0001$). 2. Pre-albumin and RBP significantly increased in Group A compared to both Group B

Author Year Country Study Design Sample Size	Methods	Outcome
	A), parenteral (Group B), or both enteral and parenteral (Group C). Those who participated were expected to stay in ICU for ≥3 days. Feeding began within 2 days of ICU admission and continued for the length of stay. **Outcome Measures:** Serum pre-albumin, Retinol-Binding Protein (RBP), nitrogen balance. Assessments were made at baseline and after (day 3, 7 and 11).	(p<0.001) and Group C (p<0.01). Significant differences in the level of pre-albumin began at day 3 (p<0.01) while the differences in the level of RBP began at day 7 (p<0.01).
Hausmann et al. (1985) Germany RCT PEDro=4 N=20	**Population:** ABI; Mean Age=28.65 yr; Gender: Male=20; GCS Range=5-7. **Intervention:** Participants were randomly assigned to one of the following feeding regimes: Total Parenteral Nutrition (TPN; n=10) or the Combined enteral-parenteral Nutrition (CN; n=10). All received maximal glucose intake of 500 g/day and sorbitol of 100 g/d. Parenteral nutrition was administered continuously via a central venous line over 24 hr. Enteral feeding was administered through a nasogastric tube at 2 hr intervals. Daily fluid balance was corrected with electrolyte solutions or through the use of diuretics. Patients were assessed up to 8 days post injury. **Outcome Measures:** Nitrogen Balance (NB), protein concentration.	1. In the CN group, 4 (40%) patients died, whereas in the TPN group, 2 (20%) patients died. The difference in mortality was not significant. 2. Regurgitated gastric fluid was lower in the TPN group compared to the CN group going into day 7 (p<0.05). 3. Protein concentration of the reflux fluid in the CN group (1.1-4.2 g/dl) was significantly elevated compared to the TPN group (0.53-0.84 g/dl) (p<0.05). 4. Regardless of the feeding regime, NB could not be reached.
Li et al. (2022) China Cohort N=61	**Population:** TBI; *Combined (PN+EN) Group (n=33):* Mean Age=51.12±11.24yr; Gender: Male=24, Female=9; Mean Time Post Injury=Not Reported; Mean GCS=7.92. *Control (PN) Group (n=28):* Mean Age=44.17±14.58yr; Gender: Male=4, Female=1; Mean Time Post Injury=Not Reported; Mean GCS=7.92. **Intervention:** Retrospective analysis of TBI patients from Xianyang Central Hospital from 2017 to 2019 that received combination of parenteral and enteral nutrition (intervention group) versus parenteral nutrition alone (control group). Outcome measures were assessed at discharge. **Outcome Measures:** ICU Length of Stay (LOS), Total Length of Stay, Total Cost of Hospitalization, Glasgow Coma Score (GCS), Long-Term Quality of Life Assessment, Complications.	1. There were no significant differences in biochemical indicators between groups. 2. Among patients with GCS≤8: Incidence of lung infection in the combined group was significantly higher than the control group (p<.001), incidence of intracranial infection, stress ulcers and diarrhea were not statistically different between groups (p=.739). 3. No significant differences were observed in hospitalization time or hospitalization costs between groups (p>.05). 4. The combined group significantly improved on GSC score (p=.042) and long-term quality of life (p=.025) compared to the control group. 5. Among patients with GCS≥9, Incidence of lung infections and intracranial infections were not statistically different between the two groups (p>.05). 6. The combined group experienced significantly greater length of hospital stay (p<.001), nasal feeding time (p<.001) and hospitalization costs (p=.006). 7. The combined group significantly improved on GSC score (p=.001) and long-term quality

Author Year Country Study Design Sample Size	Methods	Outcome
		of life (p=.015) compared to the control group.
Musillo et al. (2018) USA Case Series N=141	**Population:** TBI; Mean Age=50.8±21.14yr; Gender: Male=78.72%, Female=21.28%; Mean Time Post Injury=Not Reported; Mean GCS=9.71±4.62. **Intervention:** Retrospective analysis of individuals with TBI from Nassau University Medical Center from 2009 to 2013 that received enhanced nutritional interventions led by an interdisciplinary team including: Tube feeding pump centers, electromagnetic feeding tube placement, updated preoperative fasting policy, nutrition therapy education, enhanced protein-energy provision, modified feeding protocol **Outcome Measures:** Time to initiate nutrition therapy.	1. The majority of patients (81.56%) received enteral or parenteral nutrition, and the average time to initiation of nutrition therapy was 2.67d. 2. The average time to initiate nutrition therapy decreased each year from 2009 to 2013. 3. In 2009, the average time to initiate therapy was 3.095d. 4. In 2013, the average time to initiate therapy was 1.631d, a reduction of 47.31% 5. A significant association was found between the time to initiate nutrition and the 2012 and 2013 binary variables while controlling for confounding variables. 6. From 2009 to 2012 the time frame was 1.09d shorter (p=.008)
Fan et al. (2016a) China PCT N=40	**Population:** TBI; Mean Age=41.69 yr; Gender: Male=62, Female=58. **Intervention:** Patients were assigned to receive nutrition Enterally (EN), Parenterally (PN), or both (EN+PN), supported by nutritional therapies. Measures were taken at day 1 and day 20. **Outcome Measures:** Nutritional status, complications, clinical outcomes.	1. Total serum protein was significantly decreased in the PN group (p<0.01) compared to serum protein on day 1, whereas total serum protein was significantly increased in EN and EN+PN groups (p<0.01). 2. The EN group had significantly higher rates of diarrhea (p<0.01) compared to the PN and EN+PN group. 3. Stress ulcers were significantly higher in the PN group (p<0.01) than the other two groups. 4. The EN group had significantly higher rates of aspirated pneumonia (p<0.01). The EN group had the lowest rates of pyemia (p<0.01). 5. The EN+PN group had the lowest rates of hypoproteinemia (p<0.01) and intracranial infection (p<0.01).

Author Year Country Study Design Sample Size	Methods	Outcome
Krakau et al. (2007) Sweden Case Series N=64	**Population:** Severe TBI; N=64; Mean Age=35 yr; Gender: Male=53, Female=11; GCS Score Range=3-8. **Intervention:** Retrospective chart review of individuals with severe TBI who received Parenteral Nutrition (PN) or/and Enteral Nutrition (EN), use of gastrostomy, course of assisted feeding to understand the nutritional outcomes up to 6mo or until they were independent in nutritional administration. **Outcome Measure:** nutritional administration types and frequency, Malnutrition Occurrence (Universal Screening Tool).	1. While in intensive care, all patients received PN for mean of 19 days, and most patients (86%) also received EN which was started on average 4 days after injury. 2. Administering nutrition changes were most frequent during the first month. After 3mo, a final change had been made in 90% of patients. 3. Of the 55 patients receiving EN, 14 received a gastrostomy approximately 1mo post injury (4 patients continued to depend on gastrostomy at 6mo). 4. At 6mo, 54 (84%) patients were independent, regarding administration of nutrition. 5. Of the 56 patients assessed for malnourishment, 38 (68%) met the criteria and were considered malnourished.

Discussion

In an RCT, Zhang et al. (2020) found that EN combined with PN for individuals with TBI resulted in greater improvement in the levels of hemoglobin, albumin, pre-albumin, total protein, and the outcomes, and lower rates of adverse effects and complications, when compared to EN administration only. In a cohort study, Li et al. (2022) reported that combined EN and PN resulted in lower Incidence of lung infection and greater improvement in GCS score in patients with TBI with GCS≤8 at admission compared to PN alone.

Fan et al. (2016) conducted a PCT comparing EN versus PN versus combined EN and PN. Total serum protein, pre-albumin, and hemoglobin were significantly decreased in the PN group, which corresponds to a degradation in nutritional status; in the EN and EN+PN groups, total serum and protein levels significantly increased after nutritional treatment. Therefore, the authors suggest a combination of EN+PN to improve prognosis and nutritional status for patients post injury.

A case control conducted by Krakau et al. (2007) found that 68% of patients who had sustained an ABI showed signs of malnutrition, with their lowest body weight recorded during the second month after injury. When first admitted to hospital, all patients received PN in the intensive care unit, and most patients (86%) also received EN (Krakau et al., 2007).

In an RCT, Nataloni et al. (1999) found that patients who received EN showed significant increases in serum pre-albumin and retinol-binding protein compared to the PN or combined EN and PN (Nataloni et al., 1999). Hausmann et al. (1985) conducted a RCT to investigate the effects of combined EN and PN

compared to TPN on protein catabolism. Findings from the study noted the difference in the nitrogen balance between the two feeding regimes; however, these differences were not significant. The combination EN and PN group did have significantly higher protein concentrations compared to the TPN group, but no other relevant differences in the metabolic data or mortality between each of these intervention groups was found (Hausmann et al., 1985).

Combined nutritional intervention can be delivered to patients with ABI as part of intervention programs using an interdisciplinary approach. Musillo et al. (2018) found that the utilization of EN, PN, electromagnetic feeding tube placement, nutrition therapy education for clinicians, and modified feeding protocol, led by an interdisciplinary team considerably shortened the time to initiation of nutrition therapy in patients with TBI (Musillo et al., 2018).

Conclusions

There is level 1b evidence (Zhang et al., 2020) that EN combined with PN for individuals with TBI showed greater improvement in the levels of hemoglobin, total protein, and the outcomes, and lower rates of adverse effects and complications, when compared to just EN administration.

There is level 2 evidence (Nataloni et al., 1999) that patients post head injury treated with TPN or EN had no differences in nitrogen balance, energy expenditures, meeting nutritional goals and frequency of infections. However, enteral feeding may lead to decreased rates of hyperglycemia and diarrhea compared to parenteral nutrition.

There is level 2 evidence (Hausmann et al., 1985) that parenteral nutrition reduces the amount of regurgitated gastric fluid compared to combined enteral and parenteral nutrition; however, nitrogen balance could not be reached for either PN or combined EN and PN in patients post ABI.

There is level 2 evidence (Li et al., 2022) that combined EN and PN may lead to lower Incidence of lung infection and greater improvement in GCS score in patients with TBI with GCS≤8 at admission compared to PN alone.

There is level 2 evidence (Fan et al., 2016) that enteral feeding post ABI may increase serum protein, the rate of aspirated pneumonia and diarrhea when compared to parenteral nutrition or combined enteral-parenteral nutrition in patients post ABI.

There is level 4 evidence (Krakau et al., 2007) that combined enteral-parenteral nutrition may facilitate nutritional independence within the first six months post TBI.

There is level 4 evidence (Musillo et al., 2018) that the utilization of multiple nutritional intervention strategies and an interdisciplinary approach to treatment may result in improvement in the timely initiation of nutrition therapy in patients with TBI.

KEY POINTS

- The evidence is conflicting regarding which method of feeding (EN or PN or combined EN + PN) is optimal to deliver nitrogen, meet required energy expenditures, nutritional goals, facilitate recovery, and prevent complications (e.g., diarrhea and pneumonia) immediately post injury.
- Further research is needed to clarify the effect of combined feeding routes on nitrogen balance post ABI.
- Combined enteral-parenteral nutrition post ABI may promote nutritional independence by 6 months post injury.
- The utilization of multiple nutritional intervention strategies and an interdisciplinary approach to treatment may result in improvement in the timely initiation of nutrition therapy in patients

Other Nutritional Interventions

Zinc Supplementation

Zinc is an essential element for humans as it is important for normal nucleic acid and protein metabolism (McClain et al., 1986). Moderate zinc deficiency has been associated with cell death. Serum hypozincemia and increased urinary zinc excretions are common following head injury and are thought to be an adaptive response to inhibit the proliferation of infective organisms. Levels of serum albumin, the major transport carrier for zinc, are also markedly depressed following brain injury and likely help to explain a portion of the reductions in serum zinc levels. Urinary excretion of zinc appears to be proportional to the severity of head injury (Levenson, 2005).

TABLE 21 | Zinc Supplementation for Nutritional Management Post ABI

Author Year Country Study Design Sample Size	Methods	Outcome
Khazdouz et al. (2018) Iran RCT PEDro=9 $N_{Initial}$=100 N_{Final}=94	**Population:** Severe TBI; *Intervention Group* (n=50): Mean Age= 32.0±13.8yr; Gender: Male=46, Female=4; Mean Time Post Injury= within 24 hours; Mean GCS= 7.2±0.6. *Control Group* (n=50); Mean Age= 37.6±17.5y; Gender: Male= 40, Female=10; Mean Time Post Injury= within 24 hours; Mean GCS= 7.2±0.7. **Intervention:** Patients were randomly assigned to one of two groups. Both groups were fed through a nasogastric tube for 15 days. The intervention group received 120mg Zinc supplement in addition to standard feeding formula. The control group received a placebo in addition to standard feeding formula. Patients were assessed on day 1, 7, 16, and 28 days. **Outcome Measures:** Plasma zinc, copper, and albumin levels, 24-hour urinary zinc excretion, Sequential Organ	1. Plasma zinc levels were significantly higher in the intervention group on days 7 and 16 ($p<0.001$). 2. Plasma copper and albumin levels were not significantly different at any time points between the groups. 3. 24-hour urinary zinc excretion was significantly higher in the intervention group on day 16 ($p=0.021$). 4. Compared with the control group, there were significantly lower SOFA scores ($p=0.022$), ESR levels ($p<0.001$), CRP levels ($p<0.001$), and WBC counts ($p<0.001$) in the intervention group on day 16.

Author Year Country Study Design Sample Size	Methods	Outcome
	Failure Assessment (SOFA), Erythrocyte Sedimentation Rate (ESR), C-Reactive Protein (CRP), White Blood Cell (WBC) count, Glasgow Outcome Score (GOS), mortality rate, Length of Stay (LOS), and Glasgow Coma Scale (GCS).	5. GOS and mortality were not significantly different between groups on day 28. 6. Participants in the intervention group had significantly lower LOS compared with the control group (p=0.043). GCS was not different on day 7 between groups; however, it significantly higher in the intervention group on day 16 and day 28 (p=0.007 and p=0.005, respectively).
Young et al. (1996) USA RCT PEDro=7 N=68	**Population:** TBI; *Intervention Group (n=33)*: Mean Age=34.6yr; Gender: Male=27, Female=6; Mean GCS Score=6.4. *Control Group (n=35)*: Mean Age=35.9yr; Gender: Male=28, Female=7; Mean GCS Score=6.6. **Intervention:** Patients were randomly assigned to receive either zinc at a standard level (2.5 mg) or zinc-supplementation (12 mg) for 15 days. After 15 days, oral zinc (168 mg zinc gluconate, 22 mg elemental zinc) or matching placebo tablet were given for a total of 3mo. **Outcome Measures:** Glasgow Coma Scale (GCS), Zinc plasma Levels, Predicted Energy Expenditure (PEE), Measured Energy Expenditure (MEE), Albumin Serum levels, Thyroxine-binding Prealbumin, Retinol-Binding Protein (RBP)	1. There was no significant difference in 1mo mortality rates between groups (p=0.09). 2. GCS scores of the zinc-supplemented group were greater than the adjusted mean GCS score of the standard group at day 28 (p=0.03). 3. Mean serum pre-albumin levels and mean RBP concentrations were significantly higher in the zinc-supplementation group at 3wk post injury (p=0.003 and p=0.01, respectively). 4. The groups were not different in serum zinc concentration, weight, energy expenditure, or total urinary nitrogen excretion after admission. 5. The mean 24hr urine zinc levels were significantly greater in the zinc-supplemented group at days 2 (p=0.0001) and 10 (p=0.01).

Discussion

Two RCTs examined the effect of zinc supplementation following ABI (Khazdouz et al., 2018; Young et al., 1996). An improvement in protein synthesis and neurological recovery (measured via GCS) in patients who received supplementation was reported, in comparison to matching placebo tablet (Young et al., 1996). Surprisingly, there were no differences in either the serum or cerebrospinal fluid zinc concentrations between the groups. In contrast, Khazdouz et al. (2018) found that zinc supplementation increased GCS scores, plasma zinc concentrations, and zinc excretory concentrations. Although there were no significant differences found in terms of GOS scores or mortality, individuals in the zinc supplementation group experienced shorter LOS (Khazdouz et al., 2018).

Conclusions

There is level 1a evidence (Khazdouz et al., 2018; Young et al., 1996) that zinc supplementation may improve neurological recovery as measured by the Glasgow Coma Scale in patients post ABI.

KEY POINTS

- Zinc supplementation in the immediate post-injury period may improve neurological recovery and visceral protein concentrations, but not mortality rates, in patients with ABI.

Growth Hormone

Anabolic agents have been proposed to improve lean body mass (Behrman et al., 1995). It has been reported that GH mobilizes fat stores and enhances whole body and liver mitochondrial protein stores (Maddaiah et al., 1973; Merimee & Rabin, 1973). It is believed that GHs exert their effects via Insulin-like Growth Factor-I (IGF-I), which is synthesized in the liver (Phillips & Vassilopoulou-Sellin, 1980). Several studies in non-stressed postoperative patients have demonstrated improvements in nitrogen balance following the use of GH (Manson et al., 1988; Manson & Wilmore, 1986; Ponting et al., 1988). However, the effects of GHs on the nutritional parameters of injured patients have not been well established.

TABLE 22 | Growth Hormone Treatment for Nutritional Management Post ABI

Author Year Country Study Design Sample Size	Methods	Outcome
Hatton et al. (2006) USA RCT PEDro=7 N=97	**Population:** TBI; *Intervention Group*: Mean Age=30yr; Gender: Male=38, Female=11; Mean GCS Score=6.4. *Control Group*: Mean Age=29yr; Gender: Male=33, Female=15; Mean GCS Score=6.7. **Intervention:** Patients were randomized to receive either plasma Insulin-like Growth Factor-I (IGF-I) and Growth Hormone (GH) or placebo within 72 hr of admission to the hospital. Those in the intervention group received 0.01 mg/kg/hr IV IGF-I by continuous infusion for up to 14 days, as well as 0.05 mg/kg/day subcutaneous GH. Controls were given normal saline, but insulin was used to keep glucose concentrations <200 mg/dl. Patients also received concomitant nutritional support (enteral or parenteral). **Outcome Measures:** Glasgow Outcome Scale (GOS), Mortality, Growth Hormone (GH) levels, Serum glucose concentration, Nitrogen balance, Measured Energy Expenditure (MEE), Protein Intake, Non-protein Calorie	1. Nutritional endpoints: energy expenditure was slightly different for the two groups (2271±575.6 kcal/day in the control group and 2366±627.8 kcal/day in the intervention group). 2. In the intervention group, the mean daily glucose concentrations were higher than those of the control group (123±24 mg/dl versus 104±11mg/dl; p<0.03). 3. Within the first 24hr nitrogen balance was positive and it remained positive for the duration of the study. 4. Nitrogen balance was higher for the intervention group (p=0.0001). Neither group reached calorie or protein intake goals; groups did not differ significantly in their intake.

Author Year Country Study Design Sample Size	Methods	Outcome
	Intake, Interleukin-6 (IL)-6, Interleukin-8 (IL-8), Insulin-like Growth Factor (IGF-I) Plasma Concentrations	
Behrman et al. (1995) USA RCT PEDro=4 N=16	**Population:** TBI (n=11), SCI (n=5); Gender: Male=12, Female=4; Total Population Mean GCS score=10. *Intervention Group (n=8)*: Mean Age=23yr. *Control Group (n=8)*: Mean Age=46yr. **Intervention:** Patients were randomly allocated to receive either intramuscular Growth Hormone (GH; 0.2 mg/kg) every day or 1 mL normal saline (control) for 7-10 days. Assessments were made on days 1, 3, 7, and 10. **Outcome Measures:** Prognostic Nutritional Index (PNI), Serum Albumin concentrations, Serum Transferrin, Lymphocyte Score (LS), Calorie intake, Protein intake, Serum concentrations of Growth Hormone (GH), Nitrogen Balance, Serum glucose concentrations, Triglyceride concentrations, Fibronectin levels.	1. GH treatment did not improve nitrogen balance, glucose concentration, triglyceride concentrations or thyroid function. 2. GH significantly enhanced constitutive serum protein concentrations (transferrin: $p<0.05$, albumin: $p<0.05$). 3. Total lymphocyte count was significantly higher in the GH group than in the control group ($p<0.05$) by day 10. 4. PNI was significantly improved in the GH group compared to the control group ($p<0.05$) by day 10.
Devesa et al. (2013) Spain Pre-Post N=13	**Population:** TBI; Mean Age=26.7yr; Gender: Male=8, Female=5; Time Post Injury=2.5 mo-11 yr. **Intervention:** All individuals received growth hormone (GH) treatment maximal dose 1 mg/day, 5x/week, resting 15d every 2mo, until a maximum of 8mo and clinical rehabilitation as necessary per individual, and the patients' outcomes were assessed before and after treatment. The outcomes were also compared considering the participants' history of acquired GH-deficiency (GHD) (n=5). **Outcome Measures:** Plasma Insulin-like Growth Factor I (IGF-I), cognitive and motor improvements.	1. Plasma IGF-I values increased after GH treatment in GHD and non-GHD participants ($p<0.01$, $p<0.05$, respectively). 2. The increase in plasma IGF-I values was significantly higher in GHD than non-GHD participants ($p<0.01$). 3. In general, cognitive improvements were better than motor improvements in all participants.

Discussion

In a study conducted by Behrman et al. (1995), GH treatments administered to patients who were completely immobilized did not improve nitrogen balance. The adjuvant recombinant human GH did, however, improve constitutive serum protein concentrations and the patients' prognostic nutritional index (Behrman et al., 1995). Conversely, another RCT found that individuals who were administered IGF-I/GH had a higher nitrogen balance per day than those in the control group (1.20 ± 0.84 versus -3.90 ± 0.87) (Hatton et al., 2006). Overall, there was a sustained improvement in metabolic and nutritional status in patients with TBI. Lastly, a study conducted by Devesa et al. (2013) found that GH administration was useful when provided with proper rehabilitation.

Conclusions

There is level 1b evidence (Hatton et al., 2006) that patients post TBI treated with insulin-like growth factor-1/growth hormone had higher glucose concentrations and nitrogen balance compared to placebo.

There is level 2 evidence (Behrman et al., 1995) that growth hormone may increase serum protein, but may not be effective in improving nitrogen balance or glucose concentration in patients post head injury.

There is level 4 evidence (Devesa et al., 2013) that growth hormone may increase plasma IGF-1 values and improve cognitive abilities in patients post TBI.

KEY POINTS

- Growth hormones may enhance nutritional repletion; however, the evidence is conflicting regarding improvements in nitrogen balance, in patients post ABI.

Increased Nitrogen Feeds

Following brain injury, nitrogen losses result from the conversion of endogenous protein to energy with the extra stress demand of recovery (Grahm et al., 1989). As suggested by Quintard and Ichai (2019), sufficient nigrogen support must be provided to patients in order to prevent hypermetabolic state post ABI (Quintard & Ichai, 2019). The attainment of a positive nitrogen balance is complicated because increasing the amount of nitrogen feeding will not be retained, rather it will cause an increased amount of nitrogen excretion (Hadley et al., 1986) . Often this positive balance does not occur until the catabolic stimulus begins to subside (Hadley et al., 1986). One study examined nitrogen feeds in ABI populations and is presented in Table 23.

TABLE 23 | Nitrogen Balance for Nutritional Management Post ABI

Author Year Country Study Design Sample Size	Methods	Outcome
Twyman (1997) USA RCT PEDro=3 N=21	**Population:** TBI; Time Post-Injury= <72 hr. **Intervention:** Patients were randomly assigned to receive either tube feeding containing 1 g nitrogen/150 cal (control group; n=11) or 1 g nitrogen/90 cal (study group; n=10). **Outcome Measures:** Nitrogen Balance, calorie intake.	1. Patients receiving the high-protein tube feeding attained a significantly greater daily (p=0.006) and cumulative (p=0.04) nitrogen balance despite higher nitrogen excretions, suggesting high nitrogen feedings are required to replace high nitrogen losses following injury. 2. Both groups of patients received similar amounts of cal/kg.

Discussion

Following a brain injury, metabolic changes can influence cell turnover, use of substrate, and body composition (Twyman, 1997). The authors noted that urinary urea nitrogen levels increased by a factor of three when compared with normal levels, within 10 days following severe head injury. In this study, high-protein nitrogen feeds improved nitrogen balance daily, as well as cumulatively, over the course of the study when compared to low-protein nitrogen feeds. On average, about 5 to 10 g of urea nitrogen are excreted daily in a healthy individual; however, individuals with ABI lose a mean of 21 g urinary urea in a single day (Twyman, 1997).

Conclusions

There is level 2 evidence (Twyman, 1997) that high-protein nitrogen feedings of approximately 1 g nitrogen/90 calories may be effective for restoring nitrogen losses compared to low-protein nitrogen feedings in patients post head injury.

KEY POINTS

- High-protein nitrogen feedings may restore nitrogen losses post ABI.

Branched-Chain Amino Acids

Branched-Chain Amino Acids (BCAAs), which include leucine, valine, and isoleucine, make up roughly 35% of the human body's essential amino acids and approximately 14% of skeletal muscle amino acids (Aquilani et al., 2005). Following intake of a meal, amino acid skeletal muscle uptake is comprised of 50% or more BCAAs (Aquilani et al., 2005). Amino acids are not just nutritionally beneficial, but they may also impact cognitive function by providing substrates and increasing brain insulin availability (Aquilani et al., 2005).

TABLE 24 | Branched-Chain Amino Acid Treatment for Nutritional Management Post ABI

Author Year Country Study Design Sample Size	Methods	Outcome
Aquilani et al (2005) Italy RCT PEDro=5 N=40	**Population:** Severe TBI; *TBI Group* (n=40) (BCAA Sub-group (n=20); TBI Mean Age=32±32yr; TBI Gender: Male=40, Female=0; TBI Mean GCS=5.9; Healthy Group (n=20); Gender: Male=20, Female=0. **Intervention:** Patients were randomized to receive either 19.6 g/day IV Branched Chain Amino Acids	1. At 15 days post admission, DRS scores significantly improved in patients with a TBI compared with the control group ($p<0.02$); improvement was greater in the BCAA sub-group than in the placebo sub-group ($p<0.004$).

Author Year Country Study Design Sample Size	Methods	Outcome
	(BCAA Group) supplementation (n=20) or an iso-nitrogenous placebo (n=20) over a period of 15 days. A group of healthy patients (n=20) matched for age, sex and sedentary lifestyle served as controls for the study. **Outcome Measures:** Disability Rating Scale (DRS), plasma concentration of BCAAs: tyrosine and tryptophan.	2. Fifteen days after admission only patients given BCAA supplementation significantly improved their baseline total BCAAs, including leucine ($p<0.01$), isoleucine ($p<0.02$) and valine ($p<0.001$). 3. Level of plasma tyrosine significantly improved in the BCAA group ($p<0.01$) but remained lower than in healthy controls. 4. Plasma tryptophan concentration was higher in patients on placebo than BCAA treatment ($p<0.01$). 5. Nutritional intake and nitrogen balance tended to be higher in patients on placebo than in the BCAA group, but the difference was not significant.

Discussion

In a systematic review by Sharma et al. (2018), BCAA supplementation was found to improve clinical outcomes, such as sleep-wake cycles and cognitive functioning, in animals and humans post TBI (Sharma et al., 2018). Only one RCT has examined the effect of BCAAs on patient outcomes in an ABI population. Aquilani et al. (2005) supplemented patients with 19.6g of BCAAs daily for 15 days and found that disability rating scale scores significantly improved in the BCAA group when compared to placebo. In addition, the total amount of BCAAs at baseline significantly improved in patients receiving BCAA supplementation, including leucine, isoleucine, valine, and tyrosine (Aquilani et al., 2005).

Conclusions

There is level 2 evidence (Aquilani et al., 2005) that branched-chain amino acid supplementation may improve disability scores compared to placebo in patients post TBI.

KEY POINTS

- Branched-chain amino acid supplementation may improve disability scores in patients with ABI.

Vitamin D Supplement

After moderate to severe brain injury, a range of pathological process in the body may initiate the neurodegenerative process and cause complications after injury. Hypoxia, oxidative stress and subsequent free radicals, elevated inflammatory cytokines and subsequent acute inflammation, and

finally cell death are some of pathological process after brain injury (Lozano et al., 2015; Morganti-Kossmann et al., 2010; Schmidt et al., 2005; Werner & Engelhard, 2007). There is limited evidence on the use of Vitamin D supplementation in ABI populations.

TABLE 25 | Vitamin D Supplement for Nutritional Management Post TBI

Author Year Country Study Design Sample Size	Methods	Outcome
Sharma et al. (2020) India RCT PEDro=10 N=35	**Population:** TBI; *Intervention group* (n=20), *Control group* (n=15), Total Mean Age=36.4yr; Gender: Male=25, Female=10. **Intervention:** Patients were randomly assigned to a treatment of vitamin D (one-time oral dose of 120,000 IU, 2 tablets of 60,000 IU each) or saccharide as placebo (2 tablets of 4g each). **Outcome Measures:** Glasgow Coma Scale (GCS), level of consciousness, Glasgow Outcome Score Extended (GOSE), ICU Length of Stay, Mechanical ventilation.	1. Compared with placebo, the level of consciousness in the vitamin D group was improved (p<0.001). 2. The mean GCS score increased by 3.86 in the vitamin D group and decreased by 0.19 in the control group (P<0.0001). 3. The duration of ICU length of stay and mechanical ventilation was lower in the vitamin D group (6.19 vs. 9.07 days). 4. GOSE was higher in the vitamin D group after 14 days when compared to control (p<0.0001).

Discussion

In an RCT, Sharma et al. (2020) examined the effects of Vitamin D on early clinical outcomes and serum cytokine levels in people with moderate to severe brain injury (Sharma et al., 2020). The authors found that application of 120,000 IU vitamin D to post-TBI treatment regimens could improve outcomes, level of consciousness, and length of stay in ICU when compared to those without vitamin D in their treatment regimen.

Conclusion

There is level 1b evidence (Sharma et al., 2020) that vitamin D supplement may increase GCS and GOS scores and reduce length of stay in ICU in patients with moderate to severe TBI.

KEY POINTS

- Vitamin D supplement may increase GCS and GOS scores and reduce length of stay in ICU in patients with moderate to severe TBI.

Conclusion

Treatment of dysphagia and nutritional status post ABI remains understudied. The evidence for interventions to manage dysphagia in ABI population is considerably limited, and few studies have assessed dysphagia specifically after TBI or ABI. Studies have mostly covered heterogeneous populations including cerebrovascular accidents and neurodegenerative conditions (Howle et al., 2011), indicating the need for studies on interventions to particularly manage dysphagia in ABI populations.

Regarding the nutritional support in patients with moderate to severe ABI, although there are several available interventions to treat malnutrition post stroke, there is limited clinical evidence to support their effect specifically within an ABI population. Therefore, more high-evidence-level studies are required to demonstrate the impacts of administration methods, timing, and content of nutritional support in ABI population (Krakau et al., 2006)

Despite several discussions on benefits and complications of enteral (EN) and parenteral (PN) nutrition supports in different studies, the evidence is still conflicting to which method, EN or PN or their combination, is optimal to provide nitrogen balance and meet the energy needs and total protein levels in the ABI population. Evidence showed that early EN may be more beneficial than standard time EN, and it seems that enhancing EN could provide flexibility to meet different nutritional needs of patients; however, existing studies showed both beneficial and compromised outcomes and more evidence is required on enhanced EN to adopt this method in clinical practice (Krenitsky, 2018).

Limited studies presented other nutritional supplements for people after ABI, including a few studies that indicated the positive effects of zinc and vitamin D supplementations on outcomes after ABI. On the other hand, the limited studies on growth hormone or insulin-like growth factor-1 (IGF-1) showed conflicting effects.

This module has also shown that both nutrition and oral care are of the utmost importance when maximizing recovery gains following ABI. According to the Canadian Dental Association (2009), diabetes, hypertension, circulatory problems, cognitive and mental health impairments, and stroke are only a few of the common systemic diseases that can negatively affect individuals' oral health as they age. The Canadian Dental Association emphasizes the importance of teaching preventative habits, such as an appropriate diet and patient-specific oral hygiene techniques, to prevent infection and decay.

Further research is needed to better determine the appropriateness of generalizing post-stroke dysphagia rehabilitation practices to an ABI population, as well as the appropriate dysphagia and malnutrition interventions post ABI.

References

Adolph, M., Hailer, S., & Eckart, J. (1995). Serum phospholipid fatty acids in severely injured patients on total parenteral nutrition with medium chain/long chain triglyceride emulsions. *Ann Nutr Metab, 39*(4), 251-260.

Anthony, J. C., Anthony, T. G., Kimball, S. R., & Jefferson, L. S. (2001, Mar). Signaling pathways involved in translational control of protein synthesis in skeletal muscle by leucine. *J Nutr, 131*(3), 856s-860s. https://doi.org/10.1093/jn/131.3.856S

Aquilani, R., Iadarola, P., Contardi, A., Boselli, M., Verri, M., Pastoris, O., Boschi, F., Arcidiaco, P., & Viglio, S. (2005, Sep). Branched-chain amino acids enhance the cognitive recovery of patients with severe traumatic brain injury. *Arch Phys Med Rehabil, 86*(9), 1729-1735. https://doi.org/10.1016/j.apmr.2005.03.022

Aviv, J. E. (2000, Apr). Prospective, randomized outcome study of endoscopy versus modified barium swallow in patients with dysphagia. *Laryngoscope, 110*(4), 563-574. https://doi.org/10.1097/00005537-200004000-00008

Azim, A., Haider, A. A., Rhee, P., Verma, K., Windell, E., Jokar, T. O., Kulvatunyou, N., Meer, M., Latifi, R., & Joseph, B. (2016). Early feeds not force feeds: Enteral nutrition in traumatic brain injury. *Journal of Trauma and Acute Care Surgery, 81*(3), 520-524.

Bach, D. B., Pouget, S., Belle, K., Kilfoil, M., Alfieri, M., McEvoy, J., & Jackson, G. (1989, Fall). An integrated team approach to the management of patients with oropharyngeal dysphagia. *J Allied Health, 18*(5), 459-468.

Barquist, E., Brown, M., Cohn, S., Lundy, D., & Jackowski, J. (2001, Sep). Postextubation fiberoptic endoscopic evaluation of swallowing after prolonged endotracheal intubation: a randomized, prospective trial. *Crit Care Med, 29*(9), 1710-1713.

Bax, L., McFarlane, M., Green, E., & Miles, A. (2014, Mar). Speech-language pathologist-led fiberoptic endoscopic evaluation of swallowing: functional outcomes for patients after stroke. *J Stroke Cerebrovasc Dis, 23*(3), e195-200. https://doi.org/10.1016/j.jstrokecerebrovasdis.2013.09.031

Behrman, S. W., Kudsk, K. A., Brown, R. O., Vehe, K. L., & Wojtysiak, S. L. (1995). The effect of growth hormone on nutritional markers in enterally fed immobilized trauma patients. *JPEN J Parenter Enteral Nutr, 19*(1), 41-46.

Belafsky, P. C., Blumenfeld, L., LePage, A., & Nahrstedt, K. (2003, Nov). The accuracy of the modified Evan's blue dye test in predicting aspiration. *Laryngoscope, 113*(11), 1969-1972.

Bell, S. D. (1996, Feb). Use of Passy-Muir tracheostomy speaking valve in mechanically ventilated neurological patients. *Crit Care Nurse, 16*(1), 63-68.

Borr, C., Hielscher-Fastabend, M., & Lucking, A. (2007, Jul). Reliability and validity of cervical auscultation. *Dysphagia, 22*(3), 225-234. https://doi.org/10.1007/s00455-007-9078-3

Borzotta, A. P., Pennings, J., Papasadero, B., Paxton, J., Mardesic, S., Borzotta, R., Parrott, A., & Bledsoe, F. (1994). Enteral versus parenteral nutrition after severe closed head injury. *Journal of Trauma and Acute Care Surgery, 37*(3), 459-468.

Brady, S. L., Hildner, C. D., & Hutchins, B. F. (1999, Summer). Simultaneous videofluoroscopic swallow study and modified Evans blue dye procedure: An evaluation of blue dye visualization in cases of known aspiration. *Dysphagia, 14*(3), 146-149.

Brooke, M., Barbour, P., Cording, L., Tolan, C., Bhoomkar, A., McCall, G., Lyons, C., Hudson, J., & Johnson, S. (1989). Nutritional Status During Rehabilitation After Head Injury. *Journal of Neurologic Rehabilitation, 3*(1), 27-33. https://doi.org/10.1177/088843908900300105

Bruder, N., Lassegue, D., Pelissier, D., Graziani, N., & Francois, G. (1994, Jul). Energy expenditure and withdrawal of sedation in severe head-injured patients. *Crit Care Med, 22*(7), 1114-1119.

Buckley, C. T., Van Matre, E. T., Fischer, P. E., Minard, G., & Dickerson, R. N. J. N. i. C. P. (2021). Improvement in protein delivery for critically ill patients requiring high-dose propofol therapy and enteral nutrition. *36*(1), 212-218.

Campbell, M. (2000). *Rehabilitation for traumatic brain injury: physical therapy practice in context* (2 ed.). Churchill Livingstone

Canadian Dental Association. (2009). *Optimal health for frail older adults: Best practices along the continuum of care*.

Carnaby-Mann, G. D., & Crary, M. A. (2010, May). McNeill dysphagia therapy program: a case-control study. *Arch Phys Med Rehabil, 91*(5), 743-749. https://doi.org/10.1016/j.apmr.2010.01.013

Carnaby, G., Hankey, G. J., & Pizzi, J. (2006, Jan). Behavioural intervention for dysphagia in acute stroke: a randomised controlled trial. *Lancet Neurol, 5*(1), 31-37. https://doi.org/10.1016/s1474-4422(05)70252-0

Carnaby, G. D., LaGorio, L., Silliman, S., & Crary, M. (2020, Apr). Exercise-based swallowing intervention (McNeill Dysphagia Therapy) with adjunctive NMES to treat dysphagia post-stroke: A double-blind placebo-controlled trial. *J Oral Rehabil, 47*(4), 501-510. https://doi.org/10.1111/joor.12928

Carteron, L., Samain, E., Winiszewski, H., Blasco, G., Balon, A. S., Gilli, C., Piton, G., Capellier, G., Pili-Floury, S., & Besch, G. (2021). Semi-elemental versus polymeric formula for enteral nutrition in brain-injured critically ill patients: a randomized trial. *Critical care, 25*(1), 31.

Cerra, F. B., Benitez, M. R., Blackburn, G. L., Irwin, R. S., Jeejeebhoy, K., Katz, D. P., Pingleton, S. K., Pomposelli, J., Rombeau, J. L., Shronts, E., Wolfe, R. R., & Zaloga, G. P. (1997, Mar). Applied nutrition in ICU patients. A consensus statement of the American College of Chest Physicians. *Chest, 111*(3), 769-778. http://journal.publications.chestnet.org/data/Journals/CHEST/21745/769.pdf

Chapple, L. S., Deane, A. M., Heyland, D. K., Lange, K., Kranz, A. J., Williams, L. T., & Chapman, M. J. (2016, Dec). Energy and protein deficits throughout hospitalization in patients admitted with a traumatic brain injury. *Clin Nutr, 35*(6), 1315-1322. https://doi.org/10.1016/j.clnu.2016.02.009

Cherney, L. R., & Halper, A. S. (1996, Dec). Swallowing problems in adults with traumatic brain injury. *Semin Neurol, 16*(4), 349-353. https://doi.org/10.1055/s-2008-1040993

Cherney, L. R., Halper, A. (1989). Recovery of Oral Nutrition After Head Injury in Adults. *Journal of Head Trauma Rehabilitation, 4*(4), 42-50.

Chong, M. S., Lieu, P. K., Sitoh, Y. Y., Meng, Y. Y., & Leow, L. P. (2003, Nov). Bedside clinical methods useful as screening test for aspiration in elderly patients with recent and previous strokes. *Ann Acad Med Singapore, 32*(6), 790-794.

Chourdakis, M., Kraus, M. M., Tzellos, T., Sardeli, C., Peftoulidou, M., Vassilakos, D., & Kouvelas, D. (2012). Effect of early compared with delayed enteral nutrition on endocrine function in patients with traumatic brain injury: an open-labeled randomized trial. *JPEN J Parenter Enteral Nutr, 36*(1), 108-116.

Clayton, B. (2012, Spring). Stroke, dysphagia and oral care: what is best practice? *Alta RN, 68*(1), 26-27.

Clayton, J., Jack, C. I., Ryall, C., Tran, J., Hilal, E., & Gosney, M. (2006, Jan). Tracheal pH monitoring and aspiration in acute stroke. *Age Ageing, 35*(1), 47-53. https://doi.org/10.1093/ageing/afj007

Clifton, G. L., Robertson, C. S., Grossman, R. G., Hodge, S., Foltz, R., & Garza, C. (1984). The metabolic response to severe head injury. *Journal of Neurosurgery, 60*(4), 678-696.

Collins, M. J., & Bakheit, A. M. (1997, Sep). Does pulse oximetry reliably detect aspiration in dysphagic stroke patients? *Stroke, 28*(9), 1773-1775.

Cook, A. M., Peppard, A., & Magnuson, B. (2008, Dec-2009 Jan). Nutrition considerations in traumatic brain injury. *Nutr Clin Pract, 23*(6), 608-620. https://doi.org/10.1177/0884533608326060

Daniels, S. K., Anderson, J. A., & Willson, P. C. (2012, Mar). Valid items for screening dysphagia risk in patients with stroke: a systematic review. *Stroke, 43*(3), 892-897. https://doi.org/10.1161/strokeaha.111.640946

Daniels, S. K., McAdam, C. P., Brailey, K., & Foundas, A. L. (1997). Clinical assessment of swallowing and prediction of dysphagia severity. *American Journal of Speech-Language Pathology, 6*(4), 17-24.

Dempsey, D. T., Guenter, P., Mullen, J. L., Fairman, R., Crosby, L. O., Spielman, G., & Gennarelli, T. (1985, Feb). Energy expenditure in acute trauma to the head with and without barbiturate therapy. *Surg Gynecol Obstet, 160*(2), 128-134.

Denes, Z. (2004, Oct 7). The influence of severe malnutrition on rehabilitation in patients with severe head injury. *Disabil Rehabil, 26*(19), 1163-1165. https://doi.org/10.1080/09638280412331270380

DePippo, K. L., Holas, M. A., & Reding, M. J. (1992, Dec). Validation of the 3-oz water swallow test for aspiration following stroke. *Arch Neurol, 49*(12), 1259-1261. http://archneur.jamanetwork.com/article.aspx?articleid=592082

DePippo, K. L., Holas, M. A., & Reding, M. J. (1994, Dec). The Burke dysphagia screening test: validation of its use in patients with stroke. *Arch Phys Med Rehabil, 75*(12), 1284-1286.

Dettelbach, M. A., Gross, R. D., Mahlmann, J., & Eibling, D. E. (1995, Jul-Aug). Effect of the Passy-Muir Valve on aspiration in patients with tracheostomy. *Head Neck, 17*(4), 297-302.

Devesa, J., Reimunde, P., Devesa, P., Barberá, M., & Arce, V. (2013). Growth hormone (GH) and brain trauma. *Hormones and behavior, 63*(2), 331-344.

Dhandapani, S., Dhandapani, M., Agarwal, M., Chutani, A. M., Subbiah, V., Sharma, B. S., & Mahapatra, A. K. (2012). The prognostic significance of the timing of total enteral feeding in traumatic brain injury. *Surg Neurol Int, 3*, 31. https://doi.org/10.4103/2152-7806.93858

Dickerson, R. N., Mitchell, J. N., Morgan, L. M., Maish, G. O. r., Croce, M. A., G., M., & Brown, R. O. (2009). Disparate response to metoclopramide therapy for gastric feeding intolerance in trauma patients with and without traumatic brain injury. *JPEN J Parenter Enteral Nutr, 33*(6), 646-655.

Donzelli, J., Brady, S., Wesling, M., & Craney, M. (2001, Oct). Simultaneous modified Evans blue dye procedure and video nasal endoscopic evaluation of the swallow. *Laryngoscope, 111*(10), 1746-1750. https://doi.org/10.1097/00005537-200110000-00015

Drake, W., O'Donoghue, S., Bartram, C., Lindsay, J., & Greenwood, R. (1997, Feb). Eating in side-lying facilitates rehabilitation in neurogenic dysphagia. *Brain Inj, 11*(2), 137-142. http://www.ingentaconnect.com/content/apl/tbin/1997/00000011/00000002/art00006?token=004e14a891cd573d2570257050234a462a3144423820657c4e75477e4324576b642738d56e1181

Du, T., Jing, X., Song, S., Lu, S., Xu, L., Tong, X., & Yan, H. (2020). Therapeutic Effect of Enteral Nutrition Supplemented with Probiotics in the Treatment of Severe Craniocerebral Injury: A Systematic Review and Meta-Analysis. *World Neurosurgery, 139*, e553-e571. https://doi.org/http://dx.doi.org/10.1016/j.wneu.2020.04.083

Dziewas, R., Ritter, M., Schilling, M., Konrad, C., Oelenberg, S., Nabavi, D. G., Stogbauer, F., Ringelstein, E. B., & Ludemann, P. (2004, Jun). Pneumonia in acute stroke patients fed by nasogastric tube. *J Neurol Neurosurg Psychiatry, 75*(6), 852-856. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1739077/pdf/v075p00852.pdf

Dziewas, R., Warnecke, T., Hamacher, C., Oelenberg, S., Teismann, I., Kraemer, C., Ritter, M., Ringelstein, E. B., & Schaebitz, W. R. (2008, Jul 23). Do nasogastric tubes worsen dysphagia in patients with acute stroke? *BMC Neurol, 8*, 28. https://doi.org/10.1186/1471-2377-8-28

Elovic, E. (2000, Jun). Pharmacological therapeutics in nutritional management. *J Head Trauma Rehabil, 15*(3), 962-964. http://graphics.tx.ovid.com/ovftpdfs/FPDDNCLBMAABLL00/fs046/ovft/live/gv023/00001199/00001199-200006000-00009.pdf

Elpern, E. H., Borkgren Okonek, M., Bacon, M., Gerstung, C., & Skrzynski, M. (2000, Jul-Aug). Effect of the Passy-Muir tracheostomy speaking valve on pulmonary aspiration in adults. *Heart Lung, 29*(4), 287-293. http://www.sciencedirect.com/science/article/pii/S0147956300895448

Eskildsen, S. J., Poulsen, I., Jakobsen, D., Riberholt, C. G., & Curtis, D. J. (2021, Dec 2). Scoping review to identify and map non-pharmacological, non-surgical treatments for dysphagia following moderate-to-severe acquired brain injury. *BMJ Open, 11*(12), e053244. https://doi.org/10.1136/bmjopen-2021-053244

Evans, D. C., Corkins, M. R., Malone, A., Miller, S., Mogensen, K. M., Guenter, P., Jensen, G. L., & Committee, A. M. (2021). The use of visceral proteins as nutrition markers: an ASPEN position paper. *Nutrition in Clinical Practice, 36*(1), 22-28.

Falcão de Arruda, I. S., & de Aguilar-Nascimento, J. E. (2004). Benefits of early enteral nutrition with glutamine and probiotics in brain injury patients. *Clinical science (London, England, 106*(3), 287-292.

Fan, M., Wang, Q., Fang, W., Jiang, Y., Li, L., Sun, P., & Wang, Z. (2016a). Early Enteral Combined with Parenteral Nutrition Treatment for Severe Traumatic Brain Injury: Effects on Immune Function, Nutritional Status and Outcomes. *Chinese medical sciences journal = Chung-kuo i hsueh k'o hsueh tsa chih, 31*(4), 213-220.

Fan, M., Wang, Q., Fang, W., Jiang, Y., Li, L., Sun, P., & Wang, Z. (2016b, Nov 20). Early Enteral Combined with Parenteral Nutrition Treatment for Severe Traumatic Brain Injury: Effects on Immune Function, Nutritional Status and Outcomes. *Chin Med Sci J, 31*(4), 213-220.

Field, L. H., & Weiss, C. J. (1989, Jan-Mar). Dysphagia with head injury. *Brain Inj, 3*(1), 19-26.

Finlayson, O., Kapral, M., Hall, R., Asllani, E., Selchen, D., & Saposnik, G. (2011, Oct 04). Risk factors, inpatient care, and outcomes of pneumonia after ischemic stroke. *Neurology, 77*(14), 1338-1345. https://doi.org/10.1212/WNL.0b013e31823152b1

Giraldo-Cadavid, L. F., Leal-Leaño, L. R., Leon-Basantes, G. A., Bastidas, A. R., Garcia, R., Ovalle, S., & Abondano-Garavito, J. E. (2017, Sep). Accuracy of endoscopic and videofluoroscopic evaluations of swallowing for oropharyngeal dysphagia. *Laryngoscope, 127*(9), 2002-2010. https://doi.org/10.1002/lary.26419

Godeanu, C. S., Costea, T., Ghica, M., Lupuliasa, D., & Gird, C. E. (2020). Evidence-based use of sea buckthorn fresh juice for patients with traumatic brain injury. A pilot study. *Farmacia, 68*(3), 541-546. https://doi.org/http://dx.doi.org/10.31925/farmacia.2020.3.21

Grahm, T. W., Zadrozny, D. B., & Harrington, T. (1989). The benefits of early jejunal hyperalimentation in the head-injured patient. *Neurosurgery, 25*(5), 729-735.

Hadley, M. N., Grahm, T. W., Harrington, T., Schiller, W. R., McDermott, M. K., & Posillico, D. B. (1986). Nutritional support and neurotrauma: a critical review of early nutrition in forty-five acute head injury patients. *Neurosurgery, 19*(3), 367-373.

Halper, A. S., Cherney, L. R., Cichowski, K., & Zhang, M. (1999, Oct). Dysphagia after head trauma: the effect of cognitive-communicative impairments on functional outcomes. *J Head Trauma Rehabil, 14*(5), 486-496. http://graphics.tx.ovid.com/ovftpdfs/FPDDNCLBMAABLL00/fs046/ovft/live/gv023/00001199/00001199-199910000-00009.pdf

Hansen, T. S., Larsen, K., & Engberg, A. W. (2008, Nov). The association of functional oral intake and pneumonia in patients with severe traumatic brain injury. *Arch Phys Med Rehabil, 89*(11), 2114-2120. https://doi.org/10.1016/j.apmr.2008.04.013

Harbrecht, B. G., Moraca, R. J., Saul, M., & Courcoulas, A. P. (1998, Oct). Percutaneous endoscopic gastrostomy reduces total hospital costs in head-injured patients. *Am J Surg, 176*(4), 311-314. http://ac.els-cdn.com/S0002961098002062/1-s2.0-S0002961098002062-main.pdf?_tid=0b77309e-9d7c-11e3-8fed-00000aacb35d&acdnat=1393264364_1fd9544b80f760b8a22295c63c3f9871

Hatton, J., Kryscio, R., Ryan, M., Ott, L., & Young, B. (2006, Dec). Systemic metabolic effects of combined insulin-like growth factor-I and growth hormone therapy in patients who have sustained acute traumatic brain injury. *J Neurosurg, 105*(6), 843-852. https://doi.org/10.3171/jns.2006.105.6.843

Hausmann, D., Mosebach, K. O., Caspari, R., & Rommelsheim, K. (1985). Combined enteral-parenteral nutrition versus total parenteral nutrition in brain-injured patients: A comparative study *Intensive Care Medicine, 11*(2), 80-84.

Haynes, M. (1992). Review article: Nutrition in the severely head-injured patient. *Clinical rehabilitation, 6*(2), 153-158.

Henson, M. B., De Castro, J. M., Stringer, A. Y., & Johnson, C. (1993, Mar-Apr). Food intake by brain-injured humans who are in the chronic phase of recovery. *Brain Inj, 7*(2), 169-178.

Holas, M. A., DePippo, K. L., & Reding, M. J. (1994, Oct). Aspiration and relative risk of medical complications following stroke. *Arch Neurol, 51*(10), 1051-1053. https://doi.org/10.1001/archneur.1994.00540220099020

Horn, S. D., Kinikini, M., Moore, L. W., Hammond, F. M., Brandstater, M. E., Smout, R. J., & Barrett, R. S. (2015). Enteral Nutrition for Patients With Traumatic Brain Injury in the Rehabilitation Setting: Associations With

Patient Preinjury and Injury Characteristics and Outcomes. *Archives of physical medicine and rehabilitation, 96*(8), S245-255.

Howle, A. A., Nott, M. T., & Baguley, I. (2011). Aspiration pneumonia following severe traumatic brain injury: prevalence and risk factors for long-term mortality. *12*(3), 179-186.

Hui, X., Haider, A. H., Hashmi, Z. G., Rushing, A. P., Dhiman, N., Scott, V. K., Selvarajah, S., Haut, E. R., Efron, D. T., & Schneider, E. B. (2013, Sep). Increased risk of pneumonia among ventilated patients with traumatic brain injury: every day counts! *J Surg Res, 184*(1), 438-443. https://doi.org/10.1016/j.jss.2013.05.072

Initiative, I. D. D. S. (2018). *A global initiative to improve the lives of over 590 million people worldwide living with dysphagia*. http://iddsi.org/about-us/

Jacobs, D. G., Jacobs, D. O., Kudsk, K. A., Moore, F. A., Oswanski, M. F., Poole, G. V., Sacks, G. S., Scherer, L. T. I., Sinclair, K. E., & Group, t. E. P. M. G. W. (2004). Practice Management Guidelines for Nutritional Support of the Trauma Patient. *57*(3), 660-679. https://doi.org/10.1097/01.Ta.0000135348.48525.A0

Jakobsen, D., Poulsen, I., Schultheiss, C., Riberholt, C. G., Curtis, D. J., Petersen, T. H., & Seidl, R. O. (2019). The effect of intensified nonverbal facilitation of swallowing on dysphagia after severe acquired brain injury: A randomised controlled pilot study. *NeuroRehabilitation, 45*(4), 525-536.

Jia, K., Tong, X., & Liang, F. (2018, 2018-Jun-14). Effects of sequential nutritional support on nutritional status and expression of regulatory T lymphocyte in patients with early severe traumatic brain injury. *Neuropsychiatric Disease and Treatment, 14*, 7. https://www.lib.uwo.ca/cgi-bin/ezpauthn.cgi?url=http://search.proquest.com/docview/2071949273?accountid=15115 http://VR2PK9SX9W.search.serialssolutions.com?ctx_ver=Z39.88-2004&ctx_enc=info:ofi/enc:UTF-8&rfr_id=info:sid/ProQ%3Apsycinfo&rft_val_fmt=info:ofi/fmt:kev:mtx:journal&rft.genre=article&rft.jtitle=Neuropsychiatric+Disease+and+Treatment&rft.atitle=Effects+of+sequential+nutritional+support+on+nutritional+status+and+expression+of+regulatory+T+lymphocyte+in+patients+with+early+severe+traumatic+brain+injury&rft.au=Jia%2C+Kai%3BTong%2C+Xin%3BLiang%2C+Fang&rft.aulast=Jia&rft.aufirst=Kai&rft.date=2018-06-14&rft.volume=14&rft.issue=&rft.spage=&rft.isbn=&rft.btitle=&rft.title=Neuropsychiatric+Disease+and+Treatment&rft.issn=11766328&rft_id=info:doi/

Johnson, E. R., McKenzie, S. W., & Sievers, A. (1993, Sep). Aspiration pneumonia in stroke. *Arch Phys Med Rehabil, 74*(9), 973-976.

Jovanovic, B., Milan, Z., Markovic-Denic, L., Djuric, O., Radinovic, K., Doklestic, K., Velickovic, J., Ivancevic, N., Gregoric, P., & Pandurovic, M. J. I. J. o. I. D. (2015). Risk factors for ventilator-associated pneumonia in patients with severe traumatic brain injury in a Serbian trauma centre. *38*, 46-51.

Justo Meirelles, C. M., & de Aguilar-Nascimento, J. E. (2011). Enteral or parenteral nutrition in traumatic brain injury: a prospective randomised trial. *Nutrición Hospitalaria : Organo Oficial de La Sociedad Española de Nutrición Parenteral y Enteral, 26*(5), 1120-1124.

Kelly, T. (2010, May 19-25). Review of the evidence to support oral hygiene in stroke patients. *Nurs Stand, 24*(37), 35-38. https://doi.org/10.7748/ns2010.05.24.37.35.c7778

Khazdouz, M., Mazidi, M., Ehsaei, M. R., Ferns, G., Kengne, A. P., & Norouzy, A. R. (2018). Impact of Zinc Supplementation on the Clinical Outcomes of Patients with Severe Head Trauma: A Double-Blind Randomized Clinical Trial. *Journal of dietary supplements, 15*(1), 1-10.

Kidd, D., Lawson, J., Nesbitt, R., & MacMahon, J. (1995, Jun). The natural history and clinical consequences of aspiration in acute stroke. *Qjm, 88*(6), 409-413.

Kim, H., & Suh, Y. (2018, Apr). Changes in the dysphagia and nutritional status of patients with brain injury. *J Clin Nurs, 27*(7-8), 1581-1588. https://doi.org/10.1111/jocn.14226

Kjaersgaard, A., Nielsen, L. H., & Sjolund, B. H. (2014, Mar). Randomized trial of two swallowing assessment approaches in patients with acquired brain injury: Facial-Oral Tract Therapy versus Fibreoptic Endoscopic Evaluation of Swallowing. *Clin Rehabil, 28*(3), 243-253. https://doi.org/10.1177/0269215513500057

Kofler, M., Schiefecker, A. J., Beer, R., Gaasch, M., Rhomberg, P., Stover, J., Pfausler, B., Thomé, C., Schmutzhard, E., & Helbok, R. (2018). Enteral nutrition increases interstitial brain glucose levels in poor-grade subarachnoid hemorrhage patients. *Journal of cerebral blood flow and metabolism : official journal of the International Society of Cerebral Blood Flow and Metabolism, 38*(3), 518-527.

Kostadima, E., Kaditis, A. G., Alexopoulos, E. I., Zakynthinos, E., & Sfyras, D. (2005, Jul). Early gastrostomy reduces the rate of ventilator-associated pneumonia in stroke or head injury patients. *Eur Respir J, 26*(1), 106-111. https://doi.org/10.1183/09031936.05.00096104

Kothari, M., Madsen, V. L. F., Castrillon, E. E., Nielsen, J. F., & Svensson, P. (2018, Apr). Spontaneous jaw muscle activity in patients with acquired brain injuries-Preliminary findings. *J Prosthodont Res, 62*(2), 268-272. https://doi.org/10.1016/j.jpor.2017.05.004

Kraaijenga, S. A., van der Molen, L., Stuiver, M. M., Teertstra, H. J., Hilgers, F. J., & van den Brekel, M. W. (2015, Aug). Effects of Strengthening Exercises on Swallowing Musculature and Function in Senior Healthy Subjects: a Prospective Effectiveness and Feasibility Study. *Dysphagia, 30*(4), 392-403. https://doi.org/10.1007/s00455-015-9611-8

Krakau, K., Hansson, A., Karlsson, T., de Boussard, C. N., Tengvar, C., & Borg, J. (2007, Apr). Nutritional treatment of patients with severe traumatic brain injury during the first six months after injury. *Nutrition, 23*(4), 308-317. https://doi.org/10.1016/j.nut.2007.01.010

Krakau, K., Omne-Ponten, M., Karlsson, T., & Borg, J. J. B. I. (2006). Metabolism and nutrition in patients with moderate and severe traumatic brain injury: a systematic review. *20*(4), 345-367.

Kramer, P., Shein, D., & Napolitano, J. (2007). Rehabilitation of speech, language and swallowing disorders. In *Acquired Brain Injury* (pp. 238-258). Springer.

Krenitsky, J. (2018). Full Force Enteral Nutrition: A New Hope, or the Dark Side? A Critical Look at Enhanced Enteral Feeding Protocols. *Practical Gastroenterology, 17*(8), 16.

Kurtz, P., & Rocha, E. E. M. (2020). Nutrition Therapy, Glucose Control, and Brain Metabolism in Traumatic Brain Injury: A Multimodal Monitoring Approach. *Frontiers in Neuroscience, 14*, 190. https://doi.org/http://dx.doi.org/10.3389/fnins.2020.00190

Landesman, A., Murphy, M., Richards, J., Smyth, J., & Osakue, B. (2003). Oral hygiene in the elderly: a quality improvement initiative. *Nurs Leadersh (Tor Ont), 16*(3), 79-90.

Langmore, S. E., Terpenning, M. S., Schork, A., Chen, Y., Murray, J. T., Lopatin, D., & Loesche, W. J. (1998, Spring). Predictors of aspiration pneumonia: how important is dysphagia? *Dysphagia, 13*(2), 69-81.

Lazarus, C., & Logemann, J. A. (1987, Feb). Swallowing disorders in closed head trauma patients. *Arch Phys Med Rehabil, 68*(2), 79-84.

Lazzara, G. L., Lazarus, C., & Logemann, J. A. (1986). Impact of thermal stimulation on the triggering of the swallowing reflex.

.

Leder, S. B., & Espinosa, J. F. (2002, Summer). Aspiration risk after acute stroke: comparison of clinical examination and fiberoptic endoscopic evaluation of swallowing. *Dysphagia, 17*(3), 214-218. https://doi.org/10.1007/s00455-002-0054-7

Leslie, P., Drinnan, M. J., Zammit-Maempel, I., Coyle, J. L., Ford, G. A., & Wilson, J. A. (2007, Oct). Cervical auscultation synchronized with images from endoscopy swallow evaluations. *Dysphagia, 22*(4), 290-298. https://doi.org/10.1007/s00455-007-9084-5

Levenson, C. W. (2005). Zinc supplementation: neuroprotective or neurotoxic? *Nutrition Reviews, 63*(4), 122-125.

Li, X., Yang, Y., Ma, Z. F., Gao, S., Ning, Y., Zhao, L., He, Z., & Luo, X. J. N. n. (2022). Enteral combined with parenteral nutrition improves clinical outcomes in patients with traumatic brain injury. *25*(3), 530-536.

Lichtman, S. W., Birnbaum, I. L., Sanfilippo, M. R., Pellicone, J. T., Damon, W. J., & King, M. L. (1995, Jun). Effect of a tracheostomy speaking valve on secretions, arterial oxygenation, and olfaction: a quantitative evaluation. *J Speech Hear Res, 38*(3), 549-555.

Lim, S. H., Lieu, P. K., Phua, S. Y., Seshadri, R., Venketasubramanian, N., Lee, S. H., & Choo, P. W. (2001, Winter). Accuracy of bedside clinical methods compared with fiberoptic endoscopic examination of swallowing (FEES) in determining the risk of aspiration in acute stroke patients. *Dysphagia, 16*(1), 1-6.

Linden, P., & Siebens, A. A. (1983, Jun). Dysphagia: predicting laryngeal penetration. *Arch Phys Med Rehabil, 64*(6), 281-284.

Loan, T. (1999, Oct). Metabolic/nutritional alterations of traumatic brain injury. *Nutrition, 15*(10), 809-812. http://www.sciencedirect.com/science/article/pii/S0899900799001689

Logemann, J. A. (1983). *Evaluation and treatment of swallowing disorders*. College-Hill Press.

Logemann, J. A. (1989). Evaluation and treatment planning for the head-injured patient with oral intake disorders. *The Journal of head trauma rehabilitation, 4*(4), 24-33.

Logemann, J. A. (1991, Jun). Approaches to management of disordered swallowing. *Baillieres Clin Gastroenterol, 5*(2), 269-280.

Logemann, J. A. (1993, Fall). The dysphagia diagnostic procedure as a treatment efficacy trial. *Clin Commun Disord, 3*(4), 1-10.

Logemann, J. A. (1997, Mar). Role of the modified barium swallow in management of patients with dysphagia. *Otolaryngol Head Neck Surg, 116*(3), 335-338.

Logemann, J. A. (1998). *The evaluation and treatment of swallowing disorders*. Pro-Ed;.

Logemann, J. A. (1999, Jul-Oct). Behavioral management for oropharyngeal dysphagia. *Folia Phoniatr Logop, 51*(4-5), 199-212. https://doi.org/21497

Logemann, J. A. (2008, Nov). Treatment of oral and pharyngeal dysphagia. *Phys Med Rehabil Clin N Am, 19*(4), 803-816, ix. https://doi.org/10.1016/j.pmr.2008.06.003

Logemann, J. A. (2013). Evaluation and Treatment of Swallowing Problems. In N. D. Zasler, Katz, D. I., Zafonte, R. D. (Ed.), *Brain Injury Medicine: Principles and Practice* (2 ed.). Demos Medical Publishing.

Lozano, D., Gonzales-Portillo, G. S., Acosta, S., de la Pena, I., Tajiri, N., Kaneko, Y., Borlongan, C. V. J. N. d., & treatment. (2015). Neuroinflammatory responses to traumatic brain injury: etiology, clinical consequences, and therapeutic opportunities. 97-106.

Mackay, L. E., Morgan, A. S., & Bernstein, B. A. (1999, Apr). Swallowing disorders in severe brain injury: risk factors affecting return to oral intake. *Arch Phys Med Rehabil, 80*(4), 365-371. http://www.sciencedirect.com/science/article/pii/S000399939990271X

Maddaiah, V. T., Sharma, R. K., Balachandar, V., Rezvani, I., Collipp, P. J., & Chen, S. Y. (1973, Jun 25). Effect of growth hormone on mitochondrial protein synthesis. *J Biol Chem, 248*(12), 4263-4268. http://www.jbc.org/content/248/12/4263.full.pdf

Maddi, A., & Scannapieco, F. A. (2013, Oct). Oral biofilms, oral and periodontal infections, and systemic disease. *Am J Dent, 26*(5), 249-254.

Mandell, L. A., & Niederman, M. S. (2019, Feb 14). Aspiration Pneumonia. *N Engl J Med, 380*(7), 651-663. https://doi.org/10.1056/NEJMra1714562

Mann, G., Hankey, G. J., & Cameron, D. (2000, Sep-Oct). Swallowing disorders following acute stroke: prevalence and diagnostic accuracy. *Cerebrovasc Dis, 10*(5), 380-386. https://doi.org/16094

Manson, J. M., Smith, R. J., & Wilmore, D. W. (1988, Aug). Growth hormone stimulates protein synthesis during hypocaloric parenteral nutrition. Role of hormonal-substrate environment. *Ann Surg, 208*(2), 136-142. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1493623/pdf/annsurg00186-0026.pdf

Manson, J. M., & Wilmore, D. W. (1986, Aug). Positive nitrogen balance with human growth hormone and hypocaloric intravenous feeding. *Surgery, 100*(2), 188-197.

Manzano, J. L., Lubillo, S., Henriquez, D., Martin, J. C., Perez, M. C., & Wilson, D. J. (1993, Apr). Verbal communication of ventilator-dependent patients. *Crit Care Med, 21*(4), 512-517.

Marcotte, J., Hazelton, J. P., Arya, C., Dalton, M., Batool, A., Gaughan, J., Nguyen, L., Porter, J., & Fox, N. (2018, 01 Jul). A selective placement strategy for surgical feeding tubes benefits trauma patients. *Journal of Trauma and Acute Care Surgery, 85*(1), 135-139. http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=emedx&AN=626499013

http://vr2pk9sx9w.search.serialssolutions.com/?url_ver=Z39.88-2004&rft_val_fmt=info:ofi/fmt:kev:mtx:journal&rfr_id=info:sid/Ovid:emedx&rft.genre=article&rft_id=info:doi/10.1097%2FTA.0000000000001867&rft_id=info:pmid/&rft.issn=2163-0755&rft.volume=85&rft.issue=1&rft.spage=135&rft.pages=135-139&rft.date=2018&rft.jtitle=Journal+of+Trauma+and+Acute+Care+Surgery&rft.atitle=A+selective+placement+strategy+for+surgical+feeding+tubes+benefits+trauma+patients&rft.aulast=Marcotte

Martino, R., Pron, G., & Diamant, N. (2000, Winter). Screening for oropharyngeal dysphagia in stroke: insufficient evidence for guidelines. *Dysphagia, 15*(1), 19-30.

McCallum, S. L. (2003, Mar). The National Dysphagia Diet: implementation at a regional rehabilitation center and hospital system. *J Am Diet Assoc, 103*(3), 381-384. https://doi.org/10.1053/jada.2003.50074

McCarty, E. B., & Chao, T. N. (2021, Sep). Dysphagia and Swallowing Disorders. *Med Clin North Am, 105*(5), 939-954. https://doi.org/10.1016/j.mcna.2021.05.013

McClain, C. J., Twyman, D. L., Ott, L. G., Rapp, R. P., Tibbs, P. A., Norton, J. A., Kasarskis, E. J., Dempsey, R. J., & Young, B. (1986). Serum and urine zinc response in head-injured patients. *Serum and urine zinc response in head-injured patients, 64*(2), 224-230.

McIntosh, E. (2023, Jan-Feb 01). Dysphagia. *Home Healthc Now, 41*(1), 36-41. https://doi.org/10.1097/nhh.0000000000001134

Melotte, E., Maudoux, A., Delhalle, S., Lagier, A., Thibaut, A., Aubinet, C., Kaux, J. F., Vanhaudenhuyse, A., Ledoux, D., Laureys, S., & Gosseries, O. (2020). Swallowing in individuals with disorders of consciousness: A cohort study. *Annals of Physical and Rehabilitation Medicine*. https://doi.org/http://dx.doi.org/10.1016/j.rehab.2020.04.008

Merimee, T. J., & Rabin, D. (1973, Sep). A survey of growth hormone secretion and action. *Metabolism, 22*(9), 1235-1251. http://www.sciencedirect.com/science/article/pii/0026049573902114

Milazzo, L., Bouchard, J., & Lund, D. (1989). The swallowing process: Effects of aging and stroke. *Physical Medicine and Rehabilitation: state of the arts reviews, 3*, 489-499.

Minard, G., Kudsk, K. A., Melton, S., Patton, J. H., & Tolley, E. A. (2000). Early versus delayed feeding with an immune-enhancing diet in patients with severe head injuries. *JPEN Journal of parenteral and enteral nutrition, 24*(3), 145-149.

Morgan, A., & Ward, E. (2001). Swallowing: Neuroanatomical and physiological framework. In T. D. Murdoch BE (Ed.), *Traumatic brain injury: associated speech, language, and swallowing disorders* (pp. 313-329). Singular Publishing Group.

Morgan, A. S., & Mackay, L. E. (1999, Oct). Causes and complications associated with swallowing disorders in traumatic brain injury. *J Head Trauma Rehabil, 14*(5), 454-461. http://graphics.tx.ovid.com/ovftpdfs/FPDDNCOBGGEMKL00/fs046/ovft/live/gv023/00001199/00001199-199910000-00006.pdf

Morganti-Kossmann, C., Semple, B., Ziebell, J., Yan, E., Bye, N., & Kossmann, T. J. N. I. t. N. B. (2010). Modulation of immune response by head injury. 193-220.

Moseley, A. M., Herbert, R. D., Sherrington, C., & Maher, C. G. (2002). Evidence for physiotherapy practice: a survey of the Physiotherapy Evidence Database (PEDro). *Aust J Physiother, 48*(1), 43-49. https://doi.org/10.1016/s0004-9514(14)60281-6

Mousavi, S. N., Nematy, M., Norouzy, A., Safarian, M., Samini, F., Birjandinejad, A., Philippou, E., & Mafinejad, A. (2014). Comparison of intensive insulin therapy versus conventional glucose control in traumatic brain injury patients on parenteral nutrition: A pilot randomized clinical trial. *Journal of research in medical sciences : the official journal of Isfahan University of Medical Sciences, 19*(5), 420-425.

Muller-Lissner, S. A., Fimmel, C. J., Will, N., Muller-Duysing, W., Heinzel, F., & Blum, A. L. (1982, Dec). Effect of gastric and transpyloric tubes on gastric emptying and duodenogastric reflux. *Gastroenterology, 83*(6), 1276-1279.

Musillo, L., Grguric, L. M., Coffield, E., Aversano, F., Bosworth, J., & Batista, R. (2018). Strategies for the Enhancement of Nutrition Practice in a New York State Level 1 Trauma Center: A Hospital's Journey. *Nutrition in Clinical Practice, 33*(4), 567-575. https://doi.org/http://dx.doi.org/10.1177/0884533617724144

Nataloni, S., Gentili, P., Marini, B., Guidi, A., Marconi, P., Busco, F., & Pelaia, P. (1999). Nutritional assessment in head injured patients through the study of rapid turnover visceral proteins. *Clinical nutrition (Edinburgh, Scotland), 18*(4), 247-251.

Niederman, M. S., & Cilloniz, C. (2022, Apr). Aspiration pneumonia. *Rev Esp Quimioter, 35 Suppl 1*(Suppl 1), 73-77. https://doi.org/10.37201/req/s01.17.2022

Nishiwaki, K., Tsuji, T., Liu, M., Hase, K., Tanaka, N., & Fujiwara, T. (2005, Jul). Identification of a simple screening tool for dysphagia in patients with stroke using factor analysis of multiple dysphagia variables. *J Rehabil Med, 37*(4), 247-251. https://doi.org/10.1080/16501970510026999

Nordio, S., Burgio, F., D'Imperio, D., De Biagi, F., Cosentino, E., & Meneghello, F. (2019). Communicative and swallowing disorders in anoxic patients: A retrospective study on clinical outcomes and performance measures. *NeuroRehabilitation, 45*(4), 453-461.

Nursal, T. Z., Erdogan, B., Noyan, T., Cekinmez, M., Atalay, B., & Bilgin, N. (2007). The effect of metoclopramide on gastric emptying in traumatic brain injury. *Journal of clinical neuroscience : official journal of the Neurosurgical Society of Australasia, 14*(4), 344-348.

O'Neil-Pirozzi, T. M., Lisiecki, D. J., Jack Momose, K., Connors, J. J., & Milliner, M. P. (2003, Winter). Simultaneous modified barium swallow and blue dye tests: a determination of the accuracy of blue dye test aspiration findings. *Dysphagia, 18*(1), 32-38. https://doi.org/10.1007/s00455-002-0081-4

O'Neil-Pirozzi, T. M., Momose, K. J., Mello, J., Lepak, P., McCabe, M., Connors, J. J., & Lisiecki, D. J. (2003). Feasibility of swallowing interventions for tracheostomized individuals with severely disordered consciousness following traumatic brain injury. *Brain injury, 17*(5), 389-399.

Ohbe, H., Jo, T., Matsui, H., Fushimi, K., & Yasunaga, H. (2020). Early enteral nutrition in patients with severe traumatic brain injury: a propensity score-matched analysis using a nationwide inpatient database in Japan. *The American journal of clinical nutrition, 111*(2), 378-384.

Osawa, A., Maeshima, S., & Tanahashi, N. (2013). Water-swallowing test: screening for aspiration in stroke patients. *Cerebrovasc Dis, 35*(3), 276-281. https://doi.org/10.1159/000348683

Ott, L., Young, B., Phillips, R., & McClain, C. (1990, Apr). Brain injury and nutrition. *Nutr Clin Pract, 5*(2), 68-73.

Painter, T. J., Rickerds, J., & Alban, R. F. (2015). Immune enhancing nutrition in traumatic brain injury - A preliminary study. *International journal of surgery (London, England), 21*, 70-74.

Panther, K. (2005). The Frazier free water protocol. *Perspectives on Swallowing and Swallowing Disorders (Dysphagia), 14*(1), 4-9.

Passy-Muir Incorporated. (2004). *Passy-Muir Clinical Inservice Outline*. http://www.passy-muir.com/pdfs/inservice_outline.pdf

Passy, V., Baydur, A., Prentice, W., & Darnell-Neal, R. (1993, Jun). Passy-Muir tracheostomy speaking valve on ventilator-dependent patients. *Laryngoscope, 103*(6), 653-658. https://doi.org/10.1288/00005537-199306000-00013

Pepe, J. L., & Barba, C. A. (1999, Oct). The metabolic response to acute traumatic brain injury and implications for nutritional support. *J Head Trauma Rehabil, 14*(5), 462-474. http://graphics.tx.ovid.com/ovftpdfs/FPDDNCOBGGEMKL00/fs046/ovft/live/gv023/00001199/00001199-199910000-00007.pdf

Perry, L. (2001, Jul). Screening swallowing function of patients with acute stroke. Part one: Identification, implementation and initial evaluation of a screening tool for use by nurses. *J Clin Nurs, 10*(4), 463-473. http://onlinelibrary.wiley.com/doi/10.1046/j.1365-2702.2001.00501.x/abstract

Phillips, L. S., & Vassilopoulou-Sellin, R. (1980, Feb 14). Somatomedins (first of two parts). *N Engl J Med, 302*(7), 371-380. https://doi.org/10.1056/nejm198002143020704

Platt, J. (2001). *Dysphagia management for long-term care: a manual for nurses and other healthcare professional*. Clinical and Educational Services.

Plurad, D. S., Kim, D., Bricker, S., Lemesurier, L., Neville, A., Bongard, F., & Putnam, B. (2013, Jul). Ventilator-associated pneumonia in severe traumatic brain injury: the clinical significance of admission chest computed tomography findings. *J Surg Res, 183*(1), 371-376. https://doi.org/10.1016/j.jss.2013.01.036

Ponting, G. A., Halliday, D., Teale, J. D., & Sim, A. J. (1988, Feb 27). Postoperative positive nitrogen balance with intravenous hyponutrition and growth hormone. *Lancet, 1*(8583), 438-440.

Quintard, H., & Ichai, C. (2019). Nutritional and metabolic supplementation for the injured brain: an update. *Current Opinion in Critical Care, 25*(2), 126-131. https://doi.org/http://dx.doi.org/10.1097/MCC.0000000000000588

Rapp, R. P., Young, B., Twyman, D., Bivins, B. A., Haack, D., Tibbs, P. A., & Bean, J. R. (1983). The favorable effect of early parenteral feeding on survival in head-injured patients. *Journal of Neurosurgery, 58*(6), 906-912.

Rasley, A., Logemann, J. A., Kahrilas, P. J., Rademaker, A. W., Pauloski, B. R., & Dodds, W. J. (1993, May). Prevention of barium aspiration during videofluoroscopic swallowing studies: value of change in posture. *AJR Am J Roentgenol, 160*(5), 1005-1009. https://doi.org/10.2214/ajr.160.5.8470567

Robertson, C. S., Clifton, G. L., & Grossman, R. G. (1984, Sep). Oxygen utilization and cardiovascular function in head-injured patients. *Neurosurgery, 15*(3), 307-314.

Robertson, T., & Carter, D. (2013). Oral intensity: reducing non-ventilator-associated hospital-acquired pneumonia in care-dependent, neurologically impaired patients. *Can J Neurosci Nurs, 35*(2), 10-17.

Rosenbek, J. C., Roecker, E. B., Wood, J. L., & Robbins, J. (1996, Fall). Thermal application reduces the duration of stage transition in dysphagia after stroke. *Dysphagia, 11*(4), 225-233.

Ryu, J. S., Park, S. R., & Choi, K. H. (2004, Oct). Prediction of laryngeal aspiration using voice analysis. *Am J Phys Med Rehabil, 83*(10), 753-757. http://graphics.tx.ovid.com/ovftpdfs/FPDDNCOBGGEMKL00/fs047/ovft/live/gv024/00002060/00002060-200410000-00002.pdf

Sacks, G. S., Brown, R. O., Teague, D., Dickerson, R. N., Tolley, E. A., & Kudsk, K. A. (1995, Sep-Oct). Early nutrition support modifies immune function in patients sustaining severe head injury. *JPEN J Parenter Enteral Nutr, 19*(5), 387-392.

Sarin, J., Balasubramaniam, R., Corcoran, A. M., Laudenbach, J. M., & Stoopler, E. T. (2008, Feb). Reducing the risk of aspiration pneumonia among elderly patients in long-term care facilities through oral health interventions. *J Am Med Dir Assoc, 9*(2), 128-135. https://doi.org/10.1016/j.jamda.2007.10.003

Schmidt, O. I., Heyde, C. E., Ertel, W., & Stahel, P. F. J. B. R. R. (2005). Closed head injury—an inflammatory disease? *, 48*(2), 388-399.

Schurr, M. J., Ebner, K. A., Maser, A. L., Sperling, K. B., Helgerson, R. B., & Harms, B. (1999, May). Formal swallowing evaluation and therapy after traumatic brain injury improves dysphagia outcomes. *J Trauma, 46*(5), 817-821; discussion 821-813.

Seguin, P., Laviolle, B., Dahyot-Fizelier, C., Dumont, R., Veber, B., Gergaud, S., Asehnoune, K., Mimoz, O., Donnio, P. Y., Bellissant, E., & Malledant, Y. (2014, Jan). Effect of oropharyngeal povidone-iodine preventive oral care on ventilator-associated pneumonia in severely brain-injured or cerebral hemorrhage patients: a multicenter, randomized controlled trial. *Crit Care Med, 42*(1), 1-8. https://doi.org/10.1097/CCM.0b013e3182a2770f

Shaker, R., Easterling, C., Kern, M., Nitschke, T., Massey, B., Daniels, S., Grande, B., Kazandjian, M., & Dikeman, K. (2002, May). Rehabilitation of swallowing by exercise in tube-fed patients with pharyngeal dysphagia secondary to abnormal UES opening. *Gastroenterology, 122*(5), 1314-1321. http://www.sciencedirect.com/science/article/pii/S0016508502623133

Shaker, R., Kern, M., Bardan, E., Taylor, A., Stewart, E. T., Hoffmann, R. G., Arndorfer, R. C., Hofmann, C., & Bonnevier, J. (1997, Jun). Augmentation of deglutitive upper esophageal sphincter opening in the elderly by exercise. *Am J Physiol, 272*(6 Pt 1), G1518-1522. http://ajpgi.physiology.org/content/272/6/G1518

Sharma, B., Lawrence, D. W., & Hutchison, M. G. (2018). Branched Chain Amino Acids (BCAAs) and Traumatic Brain Injury: A Systematic Review. *Journal of Head Trauma Rehabilitation, 33*(1), 33-45.

Sharma, S., Kumar, A., Choudhary, A., Sharma, S., Khurana, L., Sharma, N., Kumar, V., & Bisht, A. J. C. D. I. (2020). Neuroprotective role of oral vitamin D supplementation on consciousness and inflammatory biomarkers in determining severity outcome in acute traumatic brain injury patients: a double-blind randomized clinical trial. *40*, 327-334.

Shiferaw, S. M., Mengistie, E. A., Aknaw, G. M., Amare, A. T., & Azanaw, K. A. (2022). Incidence and Predictors of Aspiration Pneumonia Among Traumatic Brain Injury in Northwest Ethiopia. *Open Access Emerg Med, 14*, 85-98. https://doi.org/10.2147/oaem.S335927

Smith, H. A., Lee, S. H., O'Neill, P. A., & Connolly, M. J. (2000, Nov). The combination of bedside swallowing assessment and oxygen saturation monitoring of swallowing in acute stroke: a safe and humane screening tool. *Age Ageing, 29*(6), 495-499. http://ageing.oxfordjournals.org/content/29/6/495.full.pdf

Smithard, D. G., O'Neill, P. A., Parks, C., & Morris, J. (1996, Jul). Complications and outcome after acute stroke. Does dysphagia matter? *Stroke, 27*(7), 1200-1204.

Souba, W., & Wilmore, D. (1999). Diet and nutrition in the care of the patient with surgery, trauma, and sepsis. In O. J. Shils ME, Shike M, Ross AC (Ed.), *Modern nutrition in health and disease (book)* (pp. 1589-1618). Williams and Wilkins.

Splaingard, M. L., Hutchins, B., Sulton, L. D., & Chaudhuri, G. (1988, Aug). Aspiration in rehabilitation patients: videofluoroscopy vs bedside clinical assessment. *Arch Phys Med Rehabil, 69*(8), 637-640.

Stachler, R. J., Hamlet, S. L., Choi, J., & Fleming, S. (1996, Feb). Scintigraphic quantification of aspiration reduction with the Passy-Muir valve. *Laryngoscope, 106*(2 Pt 1), 231-234.

Steele, C. M., Bailey, G. L., Polacco, R. E., Hori, S. F., Molfenter, S. M., Oshalla, M., & Yeates, E. M. (2013). Outcomes of tongue-pressure strength and accuracy training for dysphagia following acquired brain injury. *International journal of speech-language pathology, 15*(5), 492-502.

Steele, C. M., Namasivayam-MacDonald, A. M., Guida, B. T., Cichero, J. A., Duivestein, J., Hanson, B., Lam, P., & Riquelme, L. F. (2018). Creation and Initial Validation of the International Dysphagia Diet Standardisation Initiative Functional Diet Scale. *Archives of physical medicine and rehabilitation, 99*(5), 934-944. https://doi.org/10.1016/j.apmr.2018.01.012

Stroud, A. E., Lawrie, B. W., & Wiles, C. M. (2002, Sep). Inter- and intra-rater reliability of cervical auscultation to detect aspiration in patients with dysphagia. *Clin Rehabil, 16*(6), 640-645.

Suiter, D. M., McCullough, G. H., & Powell, P. W. (2003, Fall). Effects of cuff deflation and one-way tracheostomy speaking valve placement on swallow physiology. *Dysphagia, 18*(4), 284-292. https://doi.org/10.1007/s00455-003-0022-x

Sze, W. P., Yoon, W. L., Escoffier, N., & Rickard Liow, S. J. (2016, Apr). Evaluating the Training Effects of Two Swallowing Rehabilitation Therapies Using Surface Electromyography--Chin Tuck Against Resistance (CTAR) Exercise and the Shaker Exercise. *Dysphagia, 31*(2), 195-205. https://doi.org/10.1007/s00455-015-9678-2

Takizawa, C., Gemmell, E., Kenworthy, J., & Speyer, R. (2016, Jun). A Systematic Review of the Prevalence of Oropharyngeal Dysphagia in Stroke, Parkinson's Disease, Alzheimer's Disease, Head Injury, and Pneumonia. *Dysphagia, 31*(3), 434-441. https://doi.org/10.1007/s00455-016-9695-9

Talbot, A., Brady, M., Furlanetto, D. L., Frenkel, H., & Williams, B. O. (2005, Jun). Oral care and stroke units. *Gerodontology, 22*(2), 77-83. http://onlinelibrary.wiley.com/doi/10.1111/j.1741-2358.2005.00049.x/abstract

Taylor, S., & Fettes, S. (1998). Enhanced enteral nutrition in head injury: effect on the efficacy of nutritional delivery, nitrogen balance, gastric residuals and risk of pneumonia. *Journal of Human Nutrition and Dietetics, 11*(5), 391-401.

Taylor, S. J., Fettes, S. B., Jewkes, C., & Nelson, R. J. (1999, Nov). Prospective, randomized, controlled trial to determine the effect of early enhanced enteral nutrition on clinical outcome in mechanically ventilated patients suffering head injury. *Crit Care Med, 27*(11), 2525-2531. https://doi.org/https://oce-ovid-com.proxy1.lib.uwo.ca/article/00003246-199911000-00033/HTML

Teasell, R. W., McRae, M., Marchuk, Y., & Finestone, H. M. (1996, Jul). Pneumonia associated with aspiration following stroke. *Arch Phys Med Rehabil, 77*(7), 707-709. http://www.sciencedirect.com/science/article/pii/S000399939690012X

Terre, R., & Mearin, F. (2009, Apr). Evolution of tracheal aspiration in severe traumatic brain injury-related oropharyngeal dysphagia: 1-year longitudinal follow-up study. *Neurogastroenterol Motil, 21*(4), 361-369. https://doi.org/10.1111/j.1365-2982.2008.01208.x

Tolep, K., Getch, C. L., & Criner, G. J. (1996, Jan). Swallowing dysfunction in patients receiving prolonged mechanical ventilation. *Chest, 109*(1), 167-172. http://journal.publications.chestnet.org/data/Journals/CHEST/21726/167.pdf

Triggs, J., & Pandolfino, J. (2019). Recent advances in dysphagia management. *F1000Res, 8*. https://doi.org/10.12688/f1000research.18900.1

Twyman, D. (1997, Jan). Nutritional management of the critically ill neurologic patient. *Crit Care Clin, 13*(1), 39-49.

Vejdan, A. K., & Khosravi, M. (2013, Jan). BAL for pneumonia prevention in tracheostomy patients: A clinical trial study. *Pak J Med Sci, 29*(1), 148-151. https://doi.org/10.12669/pjms.291.1971

Vieira, L. V., Pedrosa, L. A. C., Souza, V. S., Paula, C. A., & Rocha, R. (2018, 01 Oct). Incidence of diarrhea and associated risk factors in patients with traumatic brain injury and enteral nutrition. *Metabolic Brain Disease, 33*(5), 1755-1760. http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=emexb&AN=623074283

http://vr2pk9sx9w.search.serialssolutions.com/?url_ver=Z39.88-2004&rft_val_fmt=info:ofi/fmt:kev:mtx:journal&rfr_id=info:sid/Ovid:emexb&rft.genre=article&rft_id=info:doi/10.1007%2Fs11011-018-0287-2&rft_id=info:pmid/30014176&rft.issn=0885-7490&rft.volume=33&rft.issue=5&rft.spage=1755&rft.pages=1755-

1760&rft.date=2018&rft.jtitle=Metabolic+Brain+Disease&rft.atitle=Incidence+of+diarrhea+and+associated+risk+factors+in+patients+with+traumatic+brain+injury+and+enteral+nutrition&rft.aulast=Vieira

https://link.springer.com/article/10.1007%2Fs11011-018-0287-2

Wan, G., Wang, L., Zhang, G., Zhang, J., Lu, Y., Li, J., & Yi, X. (2020). Effects of probiotics combined with early enteral nutrition on endothelin-1 and C-reactive protein levels and prognosis in patients with severe traumatic brain injury. *The Journal of international medical research, 48*(3), 300060519888112.

Wandrag, L., Brett, S. J., Frost, G. S., To, M., Loubo, E. A., Jackson, N. C., Umpleby, A. M., Bountziouka, V., & Hickson, M. (2019). Leucine-enriched essential amino acid supplementation in mechanically ventilated trauma patients: A feasibility study. *Trials, 20*(1), 561. https://doi.org/http://dx.doi.org/10.1186/s13063-019-3639-2

Wang, T. G., Chang, Y. C., Chen, S. Y., & Hsiao, T. Y. (2005, Apr). Pulse oximetry does not reliably detect aspiration on videofluoroscopic swallowing study. *Arch Phys Med Rehabil, 86*(4), 730-734. https://doi.org/10.1016/j.apmr.2004.10.021

Watando, A., Ebihara, S., Ebihara, T., Okazaki, T., Takahashi, H., Asada, M., & Sasaki, H. (2004, Oct). Daily oral care and cough reflex sensitivity in elderly nursing home patients. *Chest, 126*(4), 1066-1070. https://doi.org/10.1378/chest.126.4.1066

Weekes, E., & Elia, M. (1996, Jan-Feb). Observations on the patterns of 24-hour energy expenditure changes in body composition and gastric emptying in head-injured patients receiving nasogastric tube feeding. *JPEN J Parenter Enteral Nutr, 20*(1), 31-37.

Werner, C., & Engelhard, K. J. B. B. J. o. A. (2007). Pathophysiology of traumatic brain injury. *99*(1), 4-9.

Westergren, A., Ohlsson, O., & Rahm Hallberg, I. (2001, Aug). Eating difficulties, complications and nursing interventions during a period of three months after a stroke. *J Adv Nurs, 35*(3), 416-426. http://onlinelibrary.wiley.com/store/10.1046/j.1365-2648.2001.01884.x/asset/j.1365-2648.2001.01884.x.pdf?v=1&t=hs24g9kb&s=5062daabcb028f067bc10f60d39ac667f4d01d82

Wilson, R. D., & Howe, E. C. (2012, Apr). A cost-effectiveness analysis of screening methods for dysphagia after stroke. *Pm r, 4*(4), 273-282. https://doi.org/10.1016/j.pmrj.2011.09.006

Wilson, R. F., Dente, C., & Tyburski, J. G. (2001, Mar-Apr). The nutritional management of patients with head injuries. *Neurol Res, 23*(2-3), 121-128. https://doi.org/10.1179/016164101101198451

Winstein, C. J. (1983, Dec). Neurogenic dysphagia. Frequency, progression, and outcome in adults following head injury. *Phys Ther, 63*(12), 1992-1997. http://ptjournal.apta.org/content/63/12/1992.full.pdf

Yan, N., Jiang, J., Liu, H., Deng, L., Hu, Q., Sun, J., & Lv, M. (2021). Evidence-based bundled care for patients with dysphagia after severe traumatic brain injury: A randomized controlled trial. *American Journal of Translational Research 13*(7), 7819-7828.

Yanagawa, T., Bunn, F., Roberts, I., Wentz, R., & Pierro, A. (2000). Nutritional support for head-injured patients. *Cochrane Database Syst Rev*(2), Cd001530. https://doi.org/10.1002/14651858.cd001530

Yoon, W. L., Khoo, J. K., & Rickard Liow, S. J. (2014, Apr). Chin tuck against resistance (CTAR): new method for enhancing suprahyoid muscle activity using a Shaker-type exercise. *Dysphagia, 29*(2), 243-248. https://doi.org/10.1007/s00455-013-9502-9

Youmans, S. R., & Stierwalt, J. A. (2005, Summer). An acoustic profile of normal swallowing. *Dysphagia, 20*(3), 195-209. https://doi.org/10.1007/s00455-005-0013-1

Young, B., Ott, L., Haack, D., Twyman, D., Combs, D., Oexmann, J. B., Tibbs, P., & Dempsey, R. (1987, Jul). Effect of total parenteral nutrition upon intracranial pressure in severe head injury. *J Neurosurg, 67*(1), 76-80. https://doi.org/10.3171/jns.1987.67.1.0076

Young, B., Ott, L., Kasarskis, E., Rapp, R., Moles, K., Dempsey, R. J., Tibbs, P. A., Kryscio, R., & McClain, C. (1996, Jan). Zinc supplementation is associated with improved neurologic recovery rate and visceral protein levels of patients with severe closed head injury. *J Neurotrauma, 13*(1), 25-34.

Young, B., Ott, L., Norton, J., Tibbs, P., Rapp, R., McClain, C., & Dempsey, R. (1985, Nov). Metabolic and nutritional sequelae in the non-steroid treated head injury patient. *Neurosurgery, 17*(5), 784-791.

Young, B., Ott, L., Yingling, B., & McClain, C. (1992, Mar). Nutrition and brain injury. *J Neurotrauma, 9 Suppl 1*, S375-383.

Zasler, N. D., Devany, C. W., Jarman, A. L., Friedman, R., & Dinius, A. (1993). Oral hygiene following traumatic brain injury: a programme to promote dental health. *Brain injury, 7*(4), 339-345.

Zhang, Y., Liu, W., Lin, G., Qin, Z., Ren, L., & Zhong, C. (2020). Effect of enteral nutrition nursing combined with parenteral nutrition nursing intervention on nutritional status and immune function in patients with

severe craniocerebral injury. *International Journal of Clinical and Experimental Medicine, 13*(9), 6936-6944.